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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MAY 8 1954

AN APPRECIATION OF MITRAL STENOSIS*

PART I. CLINICAL FEATURES

BY

PAUL WOOD, O.B.E., M.D., F.R.C.P.

Physician-in-Charge, Cardiac Department, Brompton Hospital; Physician to the National Heart Hospital; Director of Studies, Institute of Cardiology

During the past three years mitral valve disease has been studied intensively at the Institute of Cardiology and at the Cardiac Department of the Brompton Hospital. It is the purpose of this paper to present a comprehensive review of the facts ascertained during this period. The work represents an elaboration of one of the papers opening the discussion on mitral stenosis at the European Congress of Cardiology held in London on September 9 to 12, 1952, and summarized in the Abstracts of Scientific Communications.

Material

The material comprises 150 cases submitted for operation, and another 150 which were considered unsuitable for surgical treatment. Amongst the surgical cases were four put up for repair of mitral incompetence; amongst the medical cases were 50 believed to have predominant mitral incompetence and another 32 in which mitral incompetence was thought to be as important as stenosis, if not more important. A further 50 patients have been studied, but are not included in the main series because they are awaiting either catheterization or valvotomy.

The material is analysed more fully in Table XXIII in the Summary, at the end of Part II. All cases were examined and assessed personally by the author, who was responsible for their medical care, including that before and after operation.

Method

These 300 cases were analysed in respect of 50 medical points, including those pertaining to radiography, fluoroscopy, and electrocardiography. Auscultation was often checked but rarely influenced by phonocardiography; and fluoroscopy was sometimes checked but never influenced by electrokymography. Where applicable, all cases were also analysed in respect of eight points relating to cardiac catheterization, 14 to valvotomy itself, and 20 to the subsequent course. Thus the great majority of those treated surgically were subjected to a 90-point analysis. All symptoms, measurements, and graphic patterns were graded from 0 (absent) to 4, the four positive grades representing the common English adjectives of degree—slight, moderate, considerable, and gross. If thought desirable, the moderate grade was divided into grades 2A and 2B, A being less severe than B.

Cardiac catheterization was carried out in 125 of the surgical cases, 42 of the medical, 17 of those with pure mitral incompetence, and in 23 awaiting valvotomy —that is, in a total of 207 cases. Pressures were recorded with reference to the sternal angle by means of a Sanborn electromanometer and polyviso, the oxygen consumption was measured by means of a Sanborn metabulator, and blood gas analysis using a Haldane type instrument. The left atrial pressure was obtained by wedging the catheter in a peripheral pulmonary artery as described by Lagerlöf and Werkö (1949). The tracing was accepted as an accurate record of the left atrial pressure if it was venous in form. This assumption has been proved valid in our laboratory at Brompton by Epps and Adler (1953). The data for calculating cardiac output and pulmonary resistance were obtained in quick succession, but not simultaneously. In one-third of the cases the left atrial and pulmonary artery pressures were also measured during and after standard exercise. The pulmonary vascular resistance was expressed in simple units obtained from dividing the mean pulmonary artery pressure minus the mean left atrial pressure (mm. Hg) by the pulmonary blood flow (l./min.), as explained in the section on resistance.

Nearly two-thirds of the surgical cases were operated on by Mr. R. C. Brock, who performed the first mitral valvotomy at Brompton on March 29, 1950. In the remainder, valvotomy was undertaken by Sir Clement Price-Thomas (5), Mr. Norman Barrett (14), Mr. Oswald Tubbs (3), Mr. W. P. Cleland (14), and Mr. Ian Hill (5) at the Brompton Hospital; by Professor R. Pilcher (13) at University College Hospital; and by Mr. Holmes Sellors (2) at the Middlesex Hospital.

The surgeons' observations with regard to the presence or absence of clot, mitral incompetence (before and after valvotomy), mitral calcification, mobility of the cusps, valve structure, and size of the mitral orifice before and after valvotomy were accepted without question. Direct pressures from the left atrium and pulmonary artery were recorded before and after valvotomy in about two-thirds of the cases. A biopsy from the left atrial appendage was obtained routinely, and from the lung in many cases. The post-operative physical signs and the general assessment of the situation and

*Delivered before the San Francisco Heart Association on October 29, 1953, and modified for the Strickland Goodall lecture of the Society of Apothecaries of London, March 24, 1954.

operative achievement were recorded as a routine before the surgeon's report was read. Follow-up notes were then made at intervals of three, six, or twelve months.

Incidence

In his Harveian oration of 1945, Sir John Parkinson produced statistical evidence indicating that in 1942 there were approximately 144,000 men between the ages of 18 and 44 with established heart disease in Great Britain, and that 80% of these—that is, 115,200—were rheumatic. Since the incidence of rheumatic heart disease is higher in women than in men, and since there are rather more women than men in the country, the total incidence of rheumatic heart disease in both sexes between the ages of 18 and 44 must be not fewer than 240,000. At least two-thirds of these, or 160,000, are predominantly mitral.

It is clear from the material comprising this paper that about one-half of all mitral cases—that is, 80,000 in the age group stated above—require valvotomy. At a conservative estimate, therefore, there should be approximately 3,000 valvotomies carried out in Great Britain per annum in order to cope with the situation.

Incidence of Individual Valve Involvement

It has never been quite clear what determines the relative frequency with which each particular valve is involved in rheumatism. According to Cabot (1926) the mitral valve is involved in 85%, the aortic in 44%, the tricuspid in 10 to 16%, and the pulmonary in 1 to 2%. These figures would not be seriously disputed at the present time. Various attempts have been made to correlate them with the frequency with which each valve was vascularized—for example, Gross and Kugel (1931). But Wearn *et al.* (1936), using indian ink instead of a barium gel, were unable to demonstrate any such correlation; they found blood vessels in 66% of the mitral valves studied, in 64% of the tricuspid valves, in 28% of the pulmonary, and in only 16% of the aortic. It has long seemed obvious to me that there might be a much simpler explanation for the phenomenon under discussion—that it depended on the degree of stress to which each valve was subjected. In a child of 10 the systemic blood pressure is about 100/60, the pulmonary about 15/6. Thus the load against which the mitral, aortic, tricuspid, and pulmonary valves have to work is in the proportion of 100, 60, 15, and 6 mm. Hg respectively. If the mitral valve was involved in 80% of cases the expected frequency of aortic, tricuspid, and pulmonary valve involvement would be 48, 12, and 5% respectively. This approximates very closely to Cabot's figures.

Age and Sex

The average age of patients in various groups and subgroups is presented in Table I. It was usually around 37.6 years, the average for the whole series. Surgical cases with simple mitral stenosis tended to be younger than their medical counterparts, although usually more severe; and patients with auricular fibrillation were usually considerably older than those with normal rhythm; but neither mitral incompetence nor an extreme pulmonary vascular resistance was related to age.

The sex incidence in the various types of mitral valve disease is presented in Table II. The figures confirm the well-known bias that mitral stenosis has for women and that mitral incompetence has for men. The extraordinarily high proportion of women in the group with a high pulmonary vascular resistance (*active* pulmonary hypertension in the table) may be due partly to the same sex factor that operates in primary pulmonary hypertension and partly to the fact that it is stenosis rather than incompetence which favours the development of a high resistance (see below).

TABLE I.—*Age Incidence*

	Groups			Total	M.S. Uncomplicated		M.S. M.I.		Extreme Resistance		Rhythm	
	Surg.	Med.	M.I.		Surg.	Med.	Surg.	Med.	Surg.	Med.	Normal	A.F.
Average age ..	36·8	37·5	37·2	37·6	35·4	41·5	37·6	38·8	37·6	38	33·6	41
Range ..	18–58	19–66	13–65	13–66								

TABLE II.—*Sex Incidence*

	Sex Ratio	
	Male	Female
M.S. with active pulmonary hypertension ..	1	7
„ uncomplicated	1	4
„ with trivial M.I.	1	3
„ „ serious M.I.	1	1
Mitral incompetence	3	2
All cases	1	2

History of Rheumatic Fever, Chorea, or Growing Pains

A previous history of the active rheumatic state was obtained in 68% of the whole series. In relatively pure mitral stenosis, with or without a high pulmonary vascular resistance, a history of previous rheumatism was obtained in 60%; when there was a serious degree of mitral incompetence with or without clinical stenosis, the incidence rose to 71.7%, and when more than one valve was causing trouble it was as high as 96%. Thus pure mitral stenosis would seem to be the least florid form of rheumatic heart disease.

Of those giving a previous history of the rheumatic state 45.7% had had a single attack of rheumatic fever, 31.5% recurrent attacks, 12.5% chorea alone, 4.8% both chorea and rheumatism, and 5.5% had had only subacute rheumatism or growing pains. Cases with significant mitral incompetence or multiple valve lesions were ten times more likely to have had recurrent rheumatic fever than isolated chorea; in relatively mild cases of pure mitral stenosis, on the other hand, a previous history of chorea alone was twice as common as recurrent rheumatic fever. This supports the conclusion drawn from the previous paragraph.

Life History

The chief landmarks in the life histories of all patients with symptoms are presented in Table III. The cases were divided into two groups according to whether mitral stenosis or incompetence was predominant. The figures for each grade were computed only from those cases which had completed their period in the grade under consideration by deteriorating sufficiently to enter the next grade. Thus the duration of grade IV symptoms could be assessed only from those who died from medical causes.

TABLE III.—*Life History*

	Latent period			Duration of Symptoms				From Onset Symptoms to Total Incapacity (Years)
	Age Initial Attack	Latent Period (Years)	Age Onset Symptoms	Grade 1 (Years)	Grade 2 (Years)	Grade 3 (Years)	Grade 4 (Years)	
Mitral stenosis	12	19	31	2·7 (0–17)	2·7 (0–18)	1·94 (0·5–11)	2 (0·5–4)	7·3
Mitral incompetence	12·5	20	32·5	2 (0–9)	1·1 (0–5)	2·25 (0–7)	>1 (0·3–3)	5·4

The rapid deterioration shown in the table suggests that there can be little point in delaying mitral valvotomy long in anatomically suitable cases once unmistakable symptoms of stenosis have developed; to do so is to invite complications such as embolism and to deprive patients of good physical health at a time of life when they have the right to expect it. Against operating too soon, however, are the surgical mortality of 6%, the 24% incidence of poor or indifferent results, and the possibility that stenosis may recur.

Pregnancy

In the whole series there were 83 mothers who between them had had 140 pregnancies. Cardiac symptoms had developed or increased during pregnancy in 43, but not in the other 97. On account of these symptoms two cases had been terminated at three months, one had had a hysterotomy at five months, one had been medically delivered at eight months, and two had had caesarean section; the remainder had been delivered naturally at term.

Of the 43 patients who deteriorated during pregnancy, 19 subsequently regained their previous state of health and 24 did not. Thus 24 out of 140 pregnancies, or 17%, precipitated permanent disability. In those cases in which pregnancy caused no trouble, cardiac symptoms did not develop for an average period of 10.4 years afterwards (range 1 to 28).

Cardiac symptoms developing during pregnancy were always due to pulmonary venous congestion and consisted of cough, breathlessness, orthopnoea, paroxysmal cardiac dyspnoea, or pulmonary oedema; sudden haemoptysis (pulmonary apoplexy) occurred in 12 out of the 43 cases (28%). Auricular fibrillation, systemic embolism, and congestive failure were rare complications. There was no evidence that those patients who developed symptoms during pregnancy were more or less likely to present later with a high pulmonary vascular resistance (34%) than those who did not (28%).

SPECIAL SYMPTOMS

Dyspnoea and Grading

Effort intolerance commonly due to dyspnoea was graded according to its severity as mentioned in the introduction under "Method." Patients in grade 1 were able to lead normal lives, but could not keep up with their fellows physically, although they might not be deterred from attempting to do so. They became unduly breathless on hurrying, running, walking up hills, or playing games. Patients in grade 2 were unable to run or hurry and found walking up hills difficult; they could walk indefinitely on the level, and were not orthopnoeic. To clarify the situation further this grade was usually divided into 2a and 2b. In grade 3 patients could walk only a few hundred yards on the level, and shopping and housework were carried out only with difficulty. Walking up hill was almost impossible and stairs had to be negotiated slowly. Patients who were more or less totally incapacitated were placed in grade 4; they could hardly manage 100 yards on the level and had abandoned their shopping and housework; many of them were virtually confined to bed. The majority of patients with orthopnoea, paroxysmal cardiac dyspnoea, or pulmonary oedema were in grade 3 or 4; out of respect for custom, cases with indisputable congestive heart failure were arbitrarily placed in grade 4.

Of the 150 patients selected for surgical treatment 19% were in grade 2 (all but two in grade 2b), 41% in grade 3, and 39% in grade 4. One patient with no effort intolerance was operated on because of recurring systemic embolism.

There were many patients in the medical and mitral incompetent groups who were only slightly breathless on effort or not at all, and it may be observed here that when such patients were catheterized the left atrial pressure was usually well below 10 mm. Hg with reference to the sternal angle. In striking contrast is the fact that of all the patients treated surgically there was only one with a left atrial pressure in this range, and that was the individual with recurrent embolism just mentioned. The belief that breathlessness in mitral valve disease is closely associated with pulmonary venous congestion is thus strongly supported.

Orthopnoea and Paroxysmal Cardiac Dyspnoea

Orthopnoea occurred in 69% of the surgical patients, in 30% of the medical, and in 44% of those with mitral incompetence—that is, in 53% of the whole series. The respective figures for *paroxysmal cardiac dyspnoea* were 49%, 16%, 32%, and 35%. It should be remembered that there were a number of relatively mild cases in the two medical groups.

In attempting to find out what particular factors governed the incidence of the major pulmonary venous congestive symptoms, patients with paroxysmal cardiac dyspnoea were compared with those who had neither paroxysmal cardiac dyspnoea nor orthopnoea, only cases with well-marked disability (grade 2b to grade 4) being selected for study, so that the two groups were matched in this respect. There were over 50 cases in each group.

The most important results of the analysis are shown in Table IV. It will be seen that the degree of stenosis was certainly not responsible for the difference in functional behaviour between the two groups. The left atrial pressure and the cardiac output at rest were both a little higher, and the rhythm was more often normal in those with paroxysmal dyspnoea, but these differences were not great. The pulmonary vascular resistance, on the other hand, showed a remarkable difference, the level in cases of paroxysmal dyspnoea being exactly half what it was in the others. If the figures are examined more closely it will be noticed that the important difference is confined to the extreme grade of resistance which was found nine times more frequently in those without paroxysmal dyspnoea or orthopnoea. Resistance lower than 10 units did not protect the lungs adequately.

TABLE IV

	Normal Rhythm (%)	L.A.P. mm. Hg	C.O. l./min.	Unusually Tight or Extreme Stenosis (%)	Resistance Units				
					1–3·9 %	4–5·9 %	6–9·9 %	10–30 %	Average
Pulmonary oedema (history of) ..	76	23	4·6	36	66·5	33·5	—	—	2·9
Paroxysmal cardiac dyspnoea (history of) ..	59	23	4·0	50	50	26	20	4	4·6
Cases without P.C.D. or orthopnoea ..	42	22	3·5	46	21	26	15	38	9·2
Whole surgical series ..	59	22·5	3·8	43	38·4	26	23	12·6	6·0

It may be tempting to assume that in their natural life history all cases of tight mitral stenosis sooner or later develop orthopnoea and paroxysmal cardiac dyspnoea, and that they then either die from pulmonary oedema or are protected by developing a high pulmonary vascular resistance; by obstructing the circulation proximal to the pulmonary capillaries this prevents dangerous rises of pulmonary venous pressure, so that patients are saved from drowning at the expense of a low cardiac output, and symptoms of pulmonary venous congestion are replaced by fatigue and oedema. This attractive hypothesis, however, is not properly supported by the facts. In the whole series such a life history was encountered in only six instances, or in 22% of all those with a resistance of 10 units or more. On the contrary, 78% of patients with a really high pulmonary vascular resistance had never had orthopnoea or paroxysmal cardiac dyspnoea at any stage. One is forced to conclude that if an extreme resistance is going to develop in mitral stenosis it does so relatively early in the course of the disease.

Frank Pulmonary Oedema

Manifest pulmonary oedema occurred in 11% of the surgical cases, in 2% of the medical, and in 6.5% of those with mitral incompetence, or in 7.5% of the whole series. Nearly 80% of such cases had more or less pure mitral stenosis, 15% combined stenosis and incompetence, and only 5% pure incompetence. Amongst the cases with stenosis 94% were women; in the small group with incompetence 75% were men.

The series is analysed in Table IV. The patients were distinctly younger (average age 32) than those who had never had pulmonary oedema (average age 37), and normal rhythm was more frequent. At rest, when free from attacks, the left atrial pressure averaged 23 mm. Hg, which was no higher than in the other cases; but in two or three instances, when an attack was threatened during cardiac catheterization, it was between 30 and 35 mm. Hg. The average cardiac output was relatively high (4.6 litres/minute). The pulmonary vascular resistance was remarkably low, averaging only 2.9 units, and never exceeding 5.2 units. The mitral orifice at operation was a little less tight than in the surgical series as a whole, not more tight.

It is concluded that pulmonary oedema tends to occur in relatively young women with average stenosis, when the pulmonary vascular resistance is unusually low. Sudden surges of cardiac output are possible because the pulmonary blood flow is not damped by the pulmonary resistance, and this allows extremely high pressures to develop in the pulmonary venous system. Thus, although these cases are rightly given top surgical priority, they are not necessarily *advanced* cases of mitral stenosis—rather to the contrary.

Haemoptysis

There are five kinds of haemoptysis complicating mitral valve disease: (1) the sudden unexpected profuse haemorrhage (pulmonary apoplexy); (2) blood-stained sputum associated with attacks of dyspnoea due to acute pulmonary venous congestion; (3) blood-streaked sputum associated with attacks of winter bronchitis, presumably due to a combination of bronchial inflammation and pulmonary venous congestion; (4) pink frothy sputum accompanying acute pulmonary oedema; and (5) frank haemoptysis due to pulmonary infarction.

Pulmonary Apoplexy

This was never seen in truly mild cases of mitral valve disease. Its incidence is given in Table V. By "serious cases only" in that Table are meant all the surgical cases,

TABLE V.—*Percentage Incidence of Haemoptysis*

	Whole Series				Serious Cases Only			Resistance Units		
	Surg.	Med.	M.I.	Total	M.S.	M.S., M.I.	M.I.	1–5·9	6–9·9	10–30
Pulmonary apoplexy..	24	13	13	18·3	22	33	15	25	20	12·5
Congestive haemoptysis: All cases ..	24	9	9	16·5	30	19	8·3	20	30	21
Recent cases								16	10	4
Pulmonary apoplexy, congestive haemoptysis, or both ..	44	25	20	34						
Pulmonary infarction	6	11	2	8·5						

but only those of comparable severity in the two medical groups, so that the relative importance of stenosis and incompetence might be probed. This column does in fact reveal that persons with combined lesions are particularly prone to pulmonary apoplexy.

It has often been stated, though with little factual support, that haemoptysis (meaning pulmonary apoplexy) occurs especially in cases of mitral stenosis complicated by pulmonary hypertension (e.g., Logan and Turner, 1953), presumably with the idea that it is akin to cerebral haemorrhage in essential hypertension. This statement is incorrect. Pulmonary apoplexy is rare when the pulmonary arterial resistance is really high, for the haemorrhage is venous and the high resistance tends to protect the pulmonary venous system from developing too high a pressure. This is shown in the third major column of the Table. Moreover, when haemorrhage was recorded in a case with extremely high resistance it had always occurred several years previously, at a time when the resistance may well have been lower. There was no single instance of pulmonary apoplexy occurring within a period of three years previous to the actual measurement of the high resistance. In the cases that have come to be regarded as being only partly protected (pulmonary resistance 6 to 9 units) pulmonary apoplexy had ceased in two-thirds.

Again, pulmonary apoplexy was a truly early symptom of mitral valve disease in 68% of the cases in which it occurred: it pre-dated the onset of grade 1 effort intolerance in 12.7%, initiated symptoms in 42.5%, and was an early symptom occurring within a year or so of the onset of effort breathlessness in 12.8%. It was a relatively late symptom in only one-third of the cases, occurring about half-way through the period of symptoms in 17% and being really late in 15%. The same truth was established in another way: the average duration of symptoms in all the cases with pulmonary apoplexy was 6.8 years; the average time of the onset of haemoptysis was one year after the onset of effort dyspnoea; and the average time at which haemorrhages ceased was three years before the patient was seen.

Pulmonary apoplexy was recurrent in 58% of the cases in which it occurred and was single in 42%; it was precipitated by pregnancy in 27%, and was sometimes provoked by physical effort.

This analysis suggests that sudden profuse haemoptysis in mitral stenosis is due to a venous haemorrhage occurring at a time when the pulmonary venous pressure has risen rather suddenly, and that such haemorrhages tend to cease when abrupt rises of pulmonary venous pressure are prevented by a high pulmonary vascular resistance, and also perhaps when the pulmonary veins and their anastomotic communications with the bronchial venous system have had time to hypertrophy in response to the raised pressure within them. It follows that pulmonary apoplexy is not a serious symptom, and this is borne out by the fact that it has never proved fatal in my experience. Indeed, this sort of haemorrhage may be regarded as a safety valve and is inevitably self-limiting, ceasing when the pulmonary venous pressure has fallen sufficiently. Whether the haemorrhage arises from rupture of a pulmonary vein or from rupture of a bronchial vein or broncho-pulmonary venous communication is beyond the scope of this paper (see Gilroy *et al.*, 1952).

Congestive Haemoptysis

This refers to blood-stained or blood-streaked sputum associated with attacks of severe dyspnoea. The haemoptysis is far less important than the dyspnoea. Its incidence is given in Table V. The second main column shows that, unlike pulmonary apoplexy, congestive haemoptysis favours mitral stenosis rather than combined lesions or pure mitral incompetence. In the third main column the lower set of figures refers only to cases with recent haemoptysis, and may correct a false impression that might be gained from the upper set, which refers also to blood-spitting many years ago.

It is worth noting that 44% of the surgical cases had either pulmonary apoplexy or congestive haemoptysis: one of the outstanding results of mitral valvotomy has been the abolition of these haemoptyses, which have occurred subsequently in only two cases. In one of these it was found impossible to perform a valvotomy, and in the other, which

was the first case operated on at Brompton Hospital, mitral stenosis has just recurred, the haemoptysis is very recent, and the patient has been advised to have a second operation.

Haemoptysis Associated with Winter Bronchitis

These cases were not separately analysed, because it was rarely possible to distinguish them from the congestive group. A few of them appear to have been included in Table V among the 25% with pulmonary apoplexy, congestive haemoptysis, or both, in the medical group.

Haemorrhage in Pulmonary Oedema

Whether acute pulmonary oedema is associated with *pink* frothy sputum or not is a matter of small moment, and such cases have not been specially studied.

Pulmonary Infarction

This was a less common cause of haemoptysis, as shown in Table V. It is invariably a late development, all such cases but two being totally incapacitated. Phlebothrombosis in the legs was nearly always responsible for the infarct; in only two was local thrombosis in a peripheral pulmonary artery or vein thought possible. In 58% of the cases with infarcts the pulmonary resistance was unduly high, usually extreme. Indeed, amongst the 100 medical cases there were eight deaths: seven of these were due to pulmonary embolism, and in six of them the pulmonary vascular resistance was over 10 units. Since this danger has been recognized, all high-resistance cases have been maintained on anticoagulants while awaiting valvotomy, and have been given high priority. The phlebothrombosis is attributed to the low cardiac output.

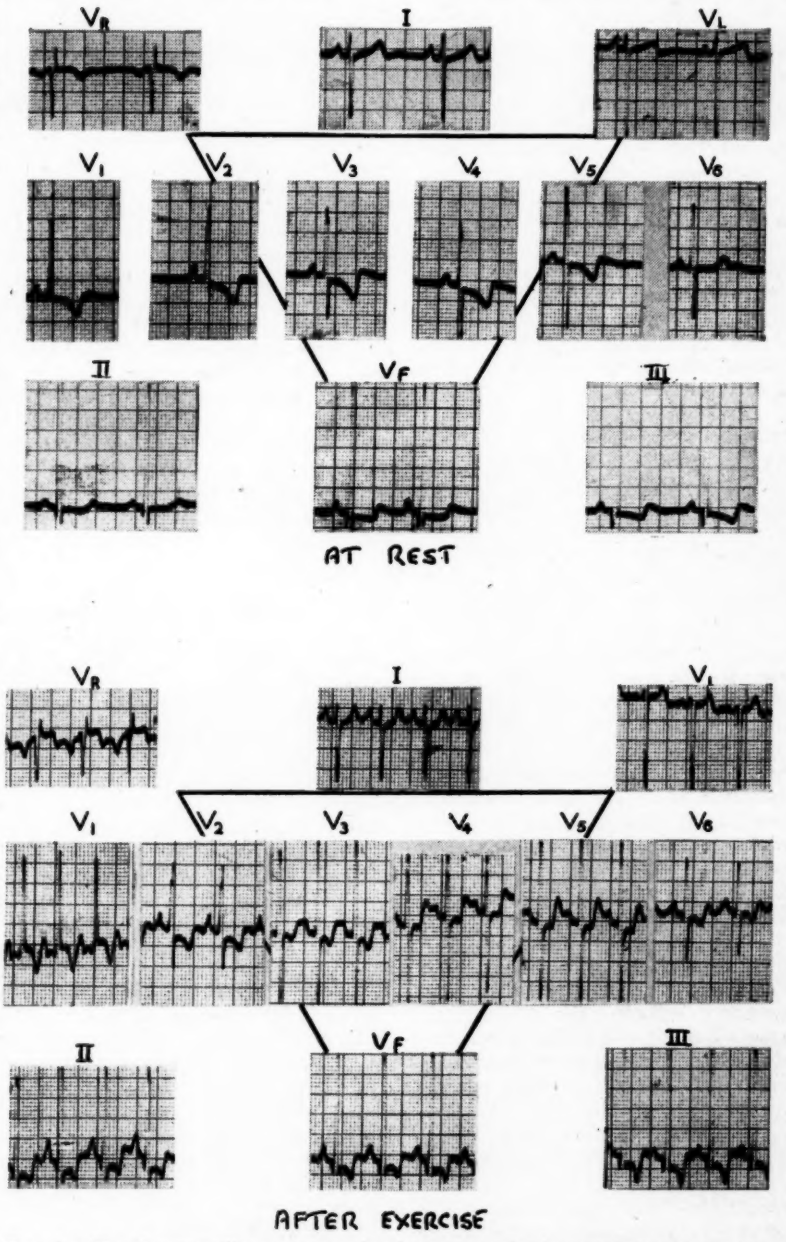

FIG. 1.—The electrocardiogram at rest and after exercise in a patient with angina pectoris complicating mitral stenosis with an extreme pulmonary vascular resistance. Note the changes in leads V_5 and V_6.

Angina Pectoris

Angina pectoris, indistinguishable in site, radiation, quality, duration of attacks, and relationship to effort from that encountered in occlusive coronary atherosclerosis, occurred in 12% of the surgical cases, 5% of the medical, and in 3% of those with almost pure mitral incompetence—that is, in 8.4% of the whole series; all of the medical cases also had serious incompetence. The average age of these patients was 36 years, or about the same as those without angina. The sex ratio was 5.5:1 in favour of women. One-third of the cases had auricular fibrillation. No significant coronary atherosclerosis was found in the four that came to necropsy. Angina disappeared in all those who had a technically successful valvotomy.

The pulmonary vascular resistance was extremely high, averaging 19.5 units, in just over a quarter of the cases, an incidence twice that in the surgical series as a whole. It is clear from Table VI, however, that angina was by no means confined to that group; a high resistance seemed to contribute to the development of angina, but was certainly not solely responsible for it.

There was some correlation between angina pectoris and the size of the mitral orifice. Thus about 40% of the cases with angina had extreme stenosis, an incidence twice as high as in the surgical series as a whole. Combined stenosis and incompetence was also twice as frequent as expected. Angina was rare in cases with virtually pure incompetence, and was not encountered at all in mild cases of any kind.

The resting electrocardiogram did not show ischaemic depression of the ST segment in any of the cases, but an ischaemic graph was sometimes obtained after effort, and the depression was then seen in left ventricular surface leads or their equivalents, even in cases with an extremely high pulmonary vascular resistance (Fig. 1).

It is believed that angina pectoris in mitral stenosis is due to functional insufficiency of the coronary blood flow resulting from strict limitation of the cardiac output, and that it is the left ventricle which suffers most. A high pulmonary resistance may encourage angina more by limiting the cardiac output than by increasing the work of the right ventricle.

TABLE VI.—*Angina Pectoris*

	Resistance Units					Size of Mitral Orifice (mm.)				
	Average	1–3·9 %	4–5·9 %	6–9·9 %	10–30 %	M.I. %	13×7 %	10×5 %	8×4 %	5×3 %
Angina pectoris ..	8	45	14	14	27	20	10	15	15	40
Whole surgical series ..	6	38	26	23	13	10	5	46	18	21
All groups (estimate)	4·2	60	20	12	8					

Systemic Embolism

A history of systemic embolism was obtained in 14% of the surgical cases, 11.5% of the medical, 9.7% of those with mitral incompetence, and in 13% of the whole series. The embolism was cerebral in 75%, peripheral in 33%, and visceral in 6%; 22% of the afflicted patients had both cerebral and peripheral emboli.

Auricular fibrillation was present in two-thirds of these cases, which is appreciably higher than in the rest of the series (Table VII). Just how often paroxysmal fibrillation was responsible for embolism in those who were regarded as having normal rhythm is unknown.

TABLE VII.—*Systemic Embolism. The Incidence of Auricular Fibrillation, Serious Mitral Incompetence, Left Atrial Dilatation, Left Atrial Thrombosis Found at Operation, and Operative Embolism in Cases Giving a History of Peripheral Embolism and in Cases Giving no such History*

	Aur. Fib. %	M.S. M.I. %	Left Atrial Dilatation. Grade		L.A. Clot at Operation %	Embolism at Operation %
			Surg. Group	All Cases		
History of embolism ..	66	44	1·74	1·86	21	10·5
No previous embolism	42	28	1·48	1·79	22·6	8

A significant degree of mitral incompetence was present more often than in cases without a history of embolism (Table VII). The influence of regurgitation on the size of the left atrium or left atrial appendage might seem to explain this; but less correlation than expected was found between the incidence of embolism and the estimated size of the left atrium (Table VII), although the figures for the surgical group may be significant.

No correlation was found between the incidence of embolism and the pulmonary vascular resistance, the cardiac output, or the size of the mitral orifice. In 12.5% of the embolic cases embolism was the first symptom, occurring at a time when there was no effort intolerance, and when the rest of the data indicated that the mitral lesion was not advanced.

At operation a clot was found in the left atrium or left atrial appendage in 21% of those who gave a history of embolism and in 23% of those who did not. Embolism was an immediate complication of mitral valvotomy in 10% of the surgical cases. A clot was detected in the left atrium in two-thirds of these. The incidence of embolism at operation was not significantly higher in those who gave a history of previous embolism than in those who did not (Table VII). Of those cases in which a clot was found in the left atrium at the time of operation one-fifth developed an embolism. This was either noticed then and there or was discovered when the patient regained consciousness in the ward. Embolism occurred only once during the post-operative course, on the third day, and has not been recorded so far at the follow-up clinic.

Several interesting conclusions can be drawn from this analysis: (1) The risk of embolism occurring at operation is almost as high as the risk of spontaneous embolism (10% compared with 13%). It is therefore unwise to advise mitral valvotomy in order to prevent future embolism in someone who has so far been free from this complication. (2) In advising mitral valvotomy to prevent a recurrence of spontaneous embolism there need be no special fear that the operation itself may cause a recurrence, the risk being no greater in those who have had previous emboli than in those who have not. (3) The infrequency of left atrial clots in patients who have given a history of embolism suggests that only fresh clots are thrown out into the circulation, and that once a clot is organized there is little danger of embolism from that source. Operative intervention alone is likely to dislodge a fragment of old thrombus.

Winter Bronchitis

Attacks of acute bronchitis, commonly in the winter, occurred in 28% of the surgical group. Its incidence was not dissimilar in medical cases of equal severity. No special correlation could be found between bronchitis and any of the other factors analysed, except that it was not a feature of mild cases. It was at first thought probable that the high incidence of bronchitis in advanced mitral valve disease depended on an excessive bronchial reaction to trivial upper respiratory tract infections because of the congested state of the bronchial mucosa. On this hypothesis the incidence of bronchitis was expected to be higher in patients with symptoms of pulmonary venous congestion than in those without. No special correlation, however, could be established. For example, the average left atrial pressure for the cases giving a history of bronchitis was 23 mm. Hg, which is practically the same as in the whole surgical group (Table VIII). Again, the incidence of bronchitis was not influenced by the pulmonary vascular resistance, although this is known to prevent excessive pulmonary venous congestion. Finally, auricular fibrillation was present rather more often in cases with bronchitis than in the controls, and it has already been shown that auricular fibrillation does not encourage pulmonary venous congestion. These negative findings do not entirely invalidate the hypothesis defined above, but seem to demand some other determinant.

TABLE VIII.—*Bronchitis*

	L.A.P. (Average) mm. Hg	Resistance Units			Aur. Fib. %	L.A. Size. Average Grade	Art. Oxygen Sat.			C.O. l./min. m⁻²
		1–5·9 %	6–9·9 %	10–30 %			96–92 %	91–88 %	87–83 %	
Bronchitis (surgical group only)	23	61	23	16	50	1·6	46	38	16	3·6
Whole surgical group	22·5	64	23	13	41	1·6	52	34	14	3·8

It is well known that great dilatation of the left atrium may compress either main bronchus and cause collapse of the lung. It was thought possible that partial bronchial compression might encourage bronchitis. The size of the left atrium in the bronchitic group was therefore compared with that in the rest of the series, but no difference was found (Table VIII); nor was bronchitis more common in cases of mitral incompetence with grade 3 dilatation of the left atrium than in cases of pure mitral stenosis with relatively small left atria.

No serious effects of recurrent bronchitis on the pulmonary circulation were detected in the majority of patients. Figures for the arterial oxygen saturation, cardiac output, and pulmonary resistance are given in Table VIII, where they are compared with figures compiled from the surgical group as a whole; there was no significant difference. It is clear that cor pulmonale does not ordinarily develop from recurrent bronchitis and emphysema associated with mitral stenosis.

One of the remarkable results of technically successful mitral valvotomy is the disappearance of winter bronchitis. This certainly supports the view that the bronchitis depends on a state of chronic pulmonary venous congestion in the majority of cases.

Auricular Fibrillation

Persistent auricular fibrillation (Table IX) occurred in 41% of the surgical cases, 40% of the medical, 30% of those with pure mitral incompetence, and 39% of the whole series; the respective figures for paroxysmal fibrillation were 5%, 7%, 6%, and 6%. Although auricular fibrillation was rather less common in those with pure mitral incompetence, it was most common when a significant degree of mitral incompetence was associated with mitral stenosis, being present in 69% of such cases.

TABLE IX.—*Auricular Fibrillation*

	Age (Yrs.)	+ve Biopsy (%)	Atrial Dilatation		Resistance Units				C.O. l./min.	Stenosis	
			L.A. Grade	R.A. Grade	Average	1–5·9 (%)	6–9·9 (%)	10–30 (%)		Mild or Average (%)	Tight or Extreme (%)
Auricular fibrillation ..	41	13	1·78	1·78	7·0	52·5	35·5	12	3·6	66	34
Normal rhythm	33·6	24	1·45	1·04	5·9	72	18·5	9·5	4·1	50	50

Patients with auricular fibrillation tended to be older than those with normal rhythm, the average age for the two groups being 41 and 33.6 respectively (surgical cases only).

The relationship of auricular fibrillation to systemic emboli has been described in a previous section. Something more should be said here, however, about *the relationship of auricular fibrillation to paroxysmal cardiac dyspnoea.* It was stated, when discussing that subject, that normal rhythm rather than auricular fibrillation favoured attacks of paroxysmal dyspnoea. There is, however, a rider to that: seven out of ten surgical cases with paroxysmal auricular fibrillation had paroxysmal cardiac dyspnoea, and in three of these cases paroxysmal auricular fibrillation was known to have precipitated the attack of dyspnoea. There is reason to believe that the sudden onset of auricular fibrillation may precipitate severe dyspnoea or right ventricular failure, according to the response of the cardiovascular system to the altered haemodynamics and to the type of case in which it occurs. When the pulmonary vascular resistance is relatively normal a sudden increase of heart rate may interfere with left ventricular diastolic filling and so increase the degree of pulmonary venous congestion (Gorlin *et al.*, 1951).

On the other hand, when the pulmonary vascular resistance is high the right ventricle is more likely to fail, particularly since it is denied the auricular support which it needs under these circumstances. Again, if the rate is too fast, even with a normal pulmonary vascular resistance, the right ventricular output may fall and so relieve pulmonary venous congestion, or a grossly irregular rhythm may have a similar effect. In short, the symptomatic pattern that results from the onset of auricular fibrillation depends on several factors which include the pulmonary vascular resistance, the rate of the heart, and the degree of irregularity of the rhythm. In cases of relatively mild mitral stenosis with attacks of dyspnoea due to paroxysmal auricular fibrillation, symptoms may be abolished by permanent digitalis therapy. This does not prevent the rhythm change, but by controlling the ventricular rate when attacks do occur it prevents the dyspnoea.

It is often stated that if auricular fibrillation occurs under the age of 20 rheumatic activity may be safely assumed. Whether this is so or not, it must not be concluded that rheumatic activity is in any way responsible for auricular fibrillation in established mitral stenosis. In the present series only 13% of cases with auricular fibrillation had positive biopsies (Aschoff nodes in the left atrial appendage), compared with 24% of those with normal rhythm. The difference is no doubt due to the age factor. Even so, the two youngest patients with auricular fibrillation (aged 18 and 23) both had negative biopsies.

It would naturally be expected that auricular fibrillation in mitral stenosis might be related to the size of the left atrium. In fact, the average size of the left atrium in the group with fibrillation was grade 1.78 compared with grade 1.45 in those with normal rhythm. This is a significant difference, but does not indicate whether the enlargement caused the fibrillation or vice versa. It should be noted, however, that the grade of right atrial enlargement was also 1.78 in the group with fibrillation and only 1.04 in the group with normal rhythm, an even greater difference. Since the right atrium is not ordinarily enlarged in mitral stenosis unless the pulmonary vascular resistance is high, it follows that atrial enlargement is more likely to be the result than the cause of auricular fibrillation, unless the latter can be shown to be closely related to pulmonary hypertension.

The pulmonary vascular resistance averaged 7.0 units in those with auricular fibrillation and 5.9 units in those with normal rhythm. Further details are given in Table IX. It may be seen that a high resistance (6 to 9 units) was nearly twice as frequent with auricular fibrillation as with normal rhythm, but the relationship did not embrace extreme resistances. The paradox may be explained by the rarity of mitral incompetence in cases with an extreme resistance. Although these figures do not deny that a dilated right atrium from pulmonary hypertension may precipitate auricular fibrillation, they are not convincing. There is no doubt that the left atrium is apt to be greatly distended in cases of combined mitral stenosis and incompetence, and auricular fibrillation is particularly common in this group. This certainly suggests that atrial dilatation can cause fibrillation. The same conclusion may be drawn from the fact that in pure mitral incompetence grade 3 or 4 left atrial dilatation occurred in 75% of those with auricular fibrillation, and in only 16.6% of those with normal rhythm.

The cardiac output tended to be lower in patients with auricular fibrillation than in those with normal rhythm, averaging 3.6 litres a minute in the former and 4.1 litres a minute in the latter (analysed from the surgical group only).

Auricular fibrillation could not be correlated directly with *the size of the mitral orifice.* Cases complicated by serious mitral incompetence were excluded from this analysis, for these are particularly prone to fibrillate and would therefore load the figures in favour of auricular fibrillation being associated with a relatively large orifice. Despite this precaution, however, cases with auricular fibrillation had unusually tight or extreme stenosis less often than cases with normal rhythm (Table IX).

The chief conclusions from these observations are that auricular fibrillation in mitral valve disease tends to be provoked by age and distension of the left atrium especially as a result of mitral incompetence, but that it also causes dilatation of both atria; it is not related to rheumatic activity or to the degree of stenosis itself. Uncontrolled auricular fibrillation may cause intense dyspnoea or congestive heart failure in cases which would not otherwise develop serious symptoms at the time.

Essential Hypertension

Only 3% of the present series had a blood pressure of 160/100 or above, and only 1% had a diastolic pressure as high as 120 mm. Hg. This figure is in harmony with Bechgaard's (1946) converse finding that only 1% of cases of essential hypertension have mitral stenosis.

PHYSICAL SIGNS

Mitral Facies

Peripheral cyanosis in the face and hands was common, and has been attributed to peripheral vasoconstriction secondary to a low cardiac output. In order to test this hypothesis, patients with the characteristic mitral facies of at least moderate degree were compared with cases in which there was no cyanosis of either face or hands. The

TABLE X.—*Mitral Facies*

	Pul. Vasc. Resistance Units	C.O. l./min.	Grade 4 Eff. Intol. (C.F.) %	Aur. Fib. %	Reduced Art. O_2 Sat. 83–89% %
Mitral facies ..	11·7	3·3	73	68	52·4
No peripheral vasoconstriction ..	4·1	4·25	9·3	25	20

results are shown in Table X, and strongly confirm the hypothesis. An extreme pulmonary vascular resistance tends to keep the output low and fixed. Grade 4 effort intolerance or complete incapacity usually means congestive heart failure proper (low output type), and auricular fibrillation also tends to keep the output low. The only other factor which seemed to contribute to the mitral facies was an arterial oxygen saturation of less than 90%.

In three cases with an extremely high pulmonary vascular resistance a bright palmar flush and hot hands were observed instead of peripheral cyanosis. This unexpected finding was attributed to hepatic dysfunction.

Peripheral Pulse

The quality of the brachial pulse was noted carefully and recorded as a routine in all cases. Quality should not be confused with amplitude (quantity). The latter was small in the great majority of all groups, being considered normal in only 11.5% of the whole series. A water-hammer quality (abrupt and collapsing) was detected in 26% of the whole series; but, whereas it was present in only 8% of the surgical cases, it was found in 29% of the medical and 84% of those with pure mitral incompetence. Again, a water-hammer pulse was recognized in only 5% of the surgical cases which were proved at operation to have no significant incompetence, whereas it was recorded in 71% of all cases with a serious degree of incompetence. It is concluded that a small water-hammer pulse is an important sign of mitral incompetence. Cases complicated by aortic incompetence were excluded from this analysis.

A careful study of routine arterial pressure tracings in many cases of mitral valve disease has confirmed this clinical observation. In cases of more or less pure stenosis the arterial tracing was blunt: the upstroke was rarely abrupt and took at least 0.08 second to reach the beginning of the summit; the summit itself was rounded and occupied about 0.07 second. The down-stroke proper was not unduly steep and rarely began before 0.15 second after the onset (Fig. 2). In mitral incompetence, on the other hand, the upstroke was often abrupt and the beginning of the summit was usually reached within 0.07 second; the peak itself was sharper, and occupied only about 0.05 second; the down-stroke proper was earlier, usually within 0.12 second after the onset and was more precipitous (Fig. 3).

The characteristic pulse of mitral incompetence may be attributed to a combination of overfilling of the left ventricle, a systolic leak into the left atrium, and a low cardiac output. Left ventricular systole is hyperdynamic and imparts an abrupt wave front to the pulse; the low resistance at the mitral orifice causes systolic collapse; the poor cardiac output results in peripheral vasoconstriction, which diminishes the amplitude of the pulse.

FIG. 2.—Intra-arterial pressure tracings from six unselected cases of mitral stenosis.

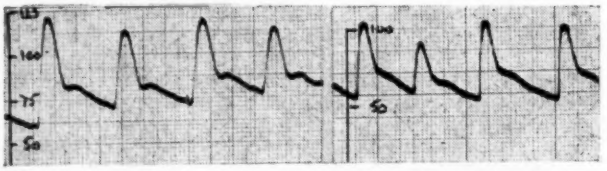

FIG. 3.—Intra-arterial pressure tracings from two cases of serious mitral incompetence. Neither had aortic incompetence.

Jugular Venous Pressure and Pulse

The jugular venous pressure was raised in 25% of the whole series. This means that the top of the oscillating venous column in the neck was at least 5 cm. of saline above the sternal angle when the patient was propped up at 30 degrees.

A giant a *wave* (Wood, 1950, 1952; Abrahams and Wood, 1951) was seen in 12 cases (4%) and always denoted an extremely high pulmonary vascular resistance (9 cases) or tricuspid stenosis (3 cases).

A combined va *wave* followed by an *x* descent, necessarily associated with sinus tachycardia, was recorded as such in five cases. None of these had a high resistance, and it is doubted if any of them were in true heart failure.

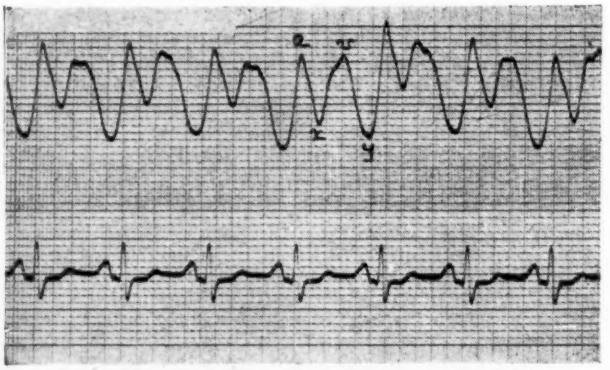

FIG. 4.—Jugular phlebogram illustrating the steep *y* descent in a patient with heart failure secondary to mitral stenosis with an extreme pulmonary vascular resistance.

This sort of venous pulse was seen in cases of severe mitral stenosis with intense pulmonary venous congestion and passive pulmonary hypertension.

a *and* v *waves of equal amplitude* were found in nine cases (3%). When the venous pressure level was around 5 cm. above the sternal angle these cases did not differ from those in the previous paragraph. When the pressure was higher, however, around 10 cm. of saline, the *v* wave was followed by a *steep y descent* which was seen only in congestive heart failure proper (Fig. 4). An extremely high pulmonary vascular resistance was responsible for the failure in the few cases of relatively pure mitral stenosis that showed this type of venous pulse; four others, however, had dominant or pure mitral incompetence, and in these the pulmonary vascular resistance was not unduly high. It is believed that some other factor operates in mitral incompetence which causes congestive heart failure with a low cardiac output in the absence of extreme pulmonary hypertension.

Mackenzie's *ventricular form of the venous pulse*, which is characterized by a single systolic wave, was recorded in

right atrial pressure tracings in all cases of auricular fibrillation and was associated with a raised venous pressure, as previously defined, in 10% of the whole series: the pulmonary vascular resistance then averaged 9 units in those with mitral stenosis; the lowest resistance was 6.4 units.

In the same group there were eight cases with a serious degree of mitral incompetence and only one of these had a high pulmonary resistance. There were also two cases with tricuspid stenosis and one with coronary embolism; the resistance was relatively normal in each of these.

Tricuspid incompetence was diagnosed when the amplitude of the *v* wave was very much greater than that ordinarily seen in normal rhythm or auricular fibrillation,

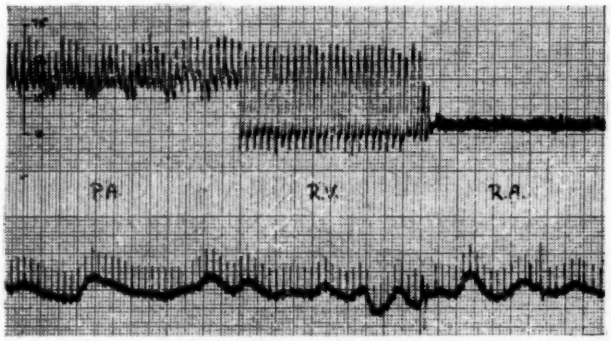

FIG. 5.—Case of tricuspid stenosis showing a diastolic pressure gradient across the tricuspid valve.

and as a rule the top of the oscillating venous column was exceptionally high. A venous pulse of this kind was seen in 6% of the whole series. Tricuspid stenosis was excluded by means of cardiac catheterization (see below). The average pulmonary vascular resistance for this group was 14.5 units, being extreme in all but three of the 18 cases and between 6 and 9 units in the exceptions. Functional tricuspid incompetence associated with mitral valve disease clearly results from right ventricular stress of a high order.

When *tricuspid stenosis* was associated with normal rhythm, a giant *a* wave was seen in the venous pulse as described above; when auricular fibrillation was present, however, there was no clinical means of recognizing tricuspid stenosis from the character of the venous pulse, but it was suspected when there were no clinical, electrocardiographic, or radiological signs of a high pulmonary vascular resistance despite a really high venous pressure; in seven such cases the presence of tricuspid stenosis was subsequently established by means of cardiac catheterization, a diastolic pressure gradient across the tricuspid valve being demonstrated when the catheter was withdrawn from the right ventricle to the right atrium (Figs. 5 and 6).

The most important conclusions to be drawn from these observations are that (1) a giant *a* wave means extreme pulmonary hypertension if the clinical signs are in harmony, or tricuspid stenosis if they are not; (2) mitral stenosis does not ordinarily cause congestive failure in the absence of a high pulmonary vascular resistance—that is, passive pulmonary hypertension does not cause congestive failure; (3) tricuspid incompetence implies a pulmonary vascular resistance in the extreme grade; (4) a high venous pressure in the absence of signs of pulmonary hypertension may well mean tricuspid stenosis; and (5) some other mechanism seems to be involved in cases of congestive heart failure associated with mitral incompetence. As a corollary to all this is the very important fact that in mitral stenosis neither congestive heart failure nor tricuspid incompetence was ever seen as the result of myocarditis itself. In other words, the so-called myocardial factor was conspicuous by its absence. In isolated or other forms of myocarditis proper, including gross rheumatic myocarditis in children, congestive heart failure is associated with a high venous pressure, a low cardiac output, and a relatively normal pulmonary vascular resistance. The only type of case in the present series in which a dominant myocardial factor has not been excluded as a cause of right ventricular failure is that with a serious degree of mitral incompetence. No further comment can be made about this possibility as yet.

Cardiac Impulse

A left ventricular thrust at the apex beat was recorded in 12% of the surgical cases, 38% of the medical, and 86% of those with pure mitral incompetence. Of the 18 cases in the surgical group, eight had a significant degree of mitral incompetence, and two had aortic stenosis. The sign was recorded erroneously in three cases in which a huge right ventricle occupied the apex of the heart; this error was suspected in view of the physical signs, but was not finally laid by the heels until the electrocardiogram was inspected. Thus there were only five cases (3.3%) in which a thrusting left ventricular impulse was unexplained. No further light was thrown on these cases as the result of valvotomy, but an enlarged left ventricle was confirmed by direct inspection of the heart. It is suspected that previous mitral incompetence may have been responsible.

Of the medical cases with this type of cardiac impulse three-fifths had a serious degree of mitral incompetence, and one-quarter had significant aortic valve disease. One patient had cardiac infarction from coronary embolism, and one had essential hypertension. There were only two cases (2%) in which the thrusting left ventricle was unexplained.

Little need be said about the 50 cases with relatively pure mitral incompetence, since 86% showed this sign. When all these cases of significant mitral incompetence in the whole series were reviewed it was found that 70% had a hyperdynamic left ventricular thrust. The importance of this sign cannot be overestimated.

There was close correlation between a left ventricular cardiac impulse and left ventricular preponderance in the electrocardiogram. Thus the electrocardiogram showed left ventricular preponderance in 48% of these cases and normal left ventricular dominance in 40%; in other words, it was left-sided in 88%. A right-sided electrocardiogram was found in 11% (only once in a case of pure mitral incompetence), and the electrocardiogram showed cardiac infarction in the case with coronary embolism.

A lift over the right ventricle, usually maximum in the third and fourth intercostal space in the left parasternal line, was appreciated in 79% of the surgical cases, in 45% of the medical, and in 36% of those with pure mitral in-

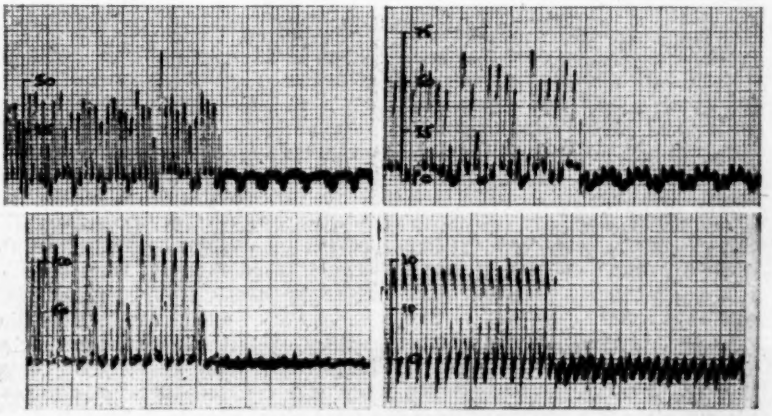

FIG. 6.—Four controls showing identical diastolic pressures in the right atrium and right ventricle.

competence, or in 61% of all cases. Since there has been a little uncertainty about the value and meaning of this sign, it was subjected to a searching cross analysis. Since the left atrium tends to be larger in cases with significant mitral incompetence than in those with pure stenosis, the figures themselves indicate that it is not the left atrium behind which is responsible for the parasternal lift in front. It was decided, therefore, to restrict the analysis to the surgical group, in which the evidence was more complete. The degree of right ventricular lift was recorded as a routine, and for the purpose of this particular analysis four groups were segregated, according to whether the lift was absent or grade 1, 2, or 3 in degree. There were 25 cases (chosen consecutively) in each group. In this way the degree of right ventricular lift was correlated with the degree of right ventricular preponderance in the electrocardiogram; the degree of dilatation of the left atrium, pulmonary artery, and right side of the heart as seen radiologically; the pulmonary vascular resistance; tricuspid incompetence; and congestive heart failure.

TABLE XI.—*Right Ventricular Lift*

R.V. Lift	R.V. Dominance (E.C.G.) Grade	Left Atrium Grade	Pulmonary Artery Grade	R. Atrium R. Ventricle Grade	Units of Resistance	T.I. %	C.F. %
0 ..	0·35	1·5	1·0	0·6	2·6	0	0
Grade 1	0·8	1·4	1·5	1·1	4·4	12	12
„ 2	1·8	1·6	2·1	1·6	6·8	12	28
„ 3 (or 4)	2·5	1·5	2·9	2·2	12·0	32	48

T.I. = Tricuspid incompetence. C.F. = Congestive heart failure.

The results are set out in Table XI. Each figure represents the average grade of the factor analysed as defined in the introduction. For example, the figure 2.9, at the bottom of the third column, represents the average grade of pulmonary artery dilatation in the 25 cases having a grade 3 (considerable) right ventricular lift. The table shows clearly that the right ventricular lift bears no relationship to the size of the left atrium, but is correlated closely with the degree of right ventricular preponderance in the electrocardiogram, with the degree of dilatation of the pulmonary artery and right side of the heart, and especially with the pulmonary vascular resistance; it was also related to the frequency of tricuspid incompetence and congestive heart failure. There can be no serious doubt that the fundamental factor which determines the degree of right ventricular thrust is the pulmonary vascular resistance.

AUSCULTATION

Presystolic Murmur

A presystolic murmur was heard in all but two of the surgical cases with normal rhythm, and there was a serious degree of mitral incompetence in the two exceptions. It was only just heard in one case in which there was an extremely high pulmonary vascular resistance. It was absent in one-third of the medical cases with normal rhythm; all but two of these had a serious degree of mitral incompetence, one had an extremely high pulmonary vascular resistance, and one was the mildest case of mitral valve disease in the whole series. It was absent in all cases classed as pure mitral incompetence. It is obvious from these figures that a presystolic murmur is excellent evidence against significant mitral incompetence. This conclusion was checked by analysing all cases of combined stenosis and incompetence in the surgical and medical groups. There were only 12 with normal rhythm, and of these only three had a presystolic murmur.

A presystolic murmur was heard in all of the six cases of mitral stenosis in which cardiac catheterization proved that the left atrial pressure (P.C.V.P.) did not exceed 10 mm. Hg with reference to the sternal angle; it was also present in all but one of the eight most trivial cases of mitral stenosis in the medical group, the exception having already been referred to above. It follows that a presystolic murmur is a sign of mitral *stenosis*, but not of its degree.

Considerable interest is attached to the effect of mitral valvotomy on the presystolic murmur. When a presystolic murmur was present before operation it was still heard afterwards in 42% of the cases, but could not be heard in 58%. One-third of the cases in which the murmur was still present were classed as excellent results, whereas two-thirds of those in which the murmur disappeared were so classed. When those cases which lost their presystolic murmur as a result of a serious degree of mitral incompetence caused by the operation were excluded from this latter group as many as 90% were classed as excellent. The significance of this will be especially appreciated in the light of the previous finding that a presystolic murmur may occur with only a trivial degree of stenosis.

First Heart Sound

The first heart sound was loud (grade 3 or 4) in 90% of cases of uncomplicated pure mitral stenosis with normal rhythm in the surgical group (Table XII). Of the exceptions, only one case had but slight accentuation and this was the mildest in the series, the left atrial pressure measuring only 10 mm. Hg and the mitral orifice measuring 1.5 cm. in length at operation. In the medical group there were 26 cases classed as mild mitral stenosis with normal rhythm; the first heart sound was markedly accentuated in 15 of them, moderately so in 6, and only slightly so in 5. In this group there were nine instances in which a loud first sound was associated with a left atrial pressure proved to be less than 10 mm. Hg.

TABLE XII

	First Heart Sound		
	Normal	Accentuated	
		Grade 1–2	Grade 3–4
M.S. mild, L.A.P. < 10 mm. ..	0	42	58
„ operated cases	0	10	90
„ *M.I.*	14	86	0
Pure M.I.	73	27	0

In the surgical group *auricular fibrillation* was present in only 14.5% of those with grade 3 accentuation of the first heart sound, but in 50% of those with grade 2 accentuation, indicating that auricular fibrillation tends to damp the intensity of the sound. In the majority of cases of auricular fibrillation the first heart sound was loud following a short diastolic period and soft after a pause, as described by Ravin and Bershof (1951). This is attributed to a tendency for the valve to close towards the end of diastole, when there is time for the ventricle to be properly filled. The absence of auricular systole favours such behaviour. In a limited number of cases, however, paradoxical accentuation of the first heart sound was noted—that is, it was softer after a short diastole and louder after a pause. No explanation for this phenomenon can yet be offered. In combined stenosis and incompetence there was usually little variation in the intensity of the first sound.

A high pulmonary vascular resistance also tended to damp the intensity of the first heart sound. Thus high or extremely high resistances were found in 25% of those with greatly accentuated first sounds, and in 41% of those with moderately accentuated first sounds. Nevertheless, extreme resistances never caused normal or soft first sounds.

Mitral incompetence was by far the most important factor modifying the first heart sound. Thus, of the surgical cases in which the degree of mitral incompetence was checked at operation, no case of significant incompetence had grade 3 accentuation of the first heart sound, 20% had grade 2 accentuation, and 66% grade 1. Again,

no case of significant mitral incompetence in the whole series had considerable accentuation of the first heart sound, 27% had grade 1 or 2 accentuation, and 73% had a normal or soft first sound. These figures were taken only from the cases without obvious calcification of the valve so that they would not be influenced by that factor. There were only three examples of marked calcification of the mitral valve without incompetence, and each of these had slight accentuation of the first heart sound. It follows that, although calcium alone may diminish the intensity of the sound, the soft first sound of mitral incompetence does not depend on its presence. As expected, there was a positive correlation between the intensity of the first heart sound and the presence and intensity of the opening snap.

It is believed that the first heart sound is loud in mitral stenosis because there is a sufficient pressure gradient across the mitral valve to billow the cusps deeply into the left ventricle right up to the moment when that chamber contracts. When there is no stenosis the left ventricle fills rapidly, so that towards the end of diastole, even when quite short, the mitral cusps tend to float into apposition, and therefore shut more quietly when the ventricle contracts (Dock, 1933). Normal rhythm favours accentuation of the first sound by increasing the pressure gradient across the valve at the end of ventricular diastole; a high pulmonary vascular resistance may damp the sound a little by encouraging the right ventricle to form the apex beat of the heart; mitral incompetence results in quicker left ventricular filling, and the rapid equalization of left atrial and left ventricular diastolic pressures may float mobile cusps into apposition before the ventricle contracts; moreover, mitral incompetence is often associated with rigid cusps, particularly in the presence of heavy calcification, and in these cases there may be little movement.

The effect of valvotomy on the intensity of the first heart sound was studied (Table XIII). When the first sound was greatly diminished after the operation 81.5% did excellently, whereas when it was unchanged or only slightly diminished only 20 to 30% did as well. When the first heart sound became soft as the result of mitral incompetence caused or increased by the valvotomy the result was poor or only fair in as many as two-thirds, and it was excellent in none. When it is remembered that the first heart sound is usually loud in trivial degrees of mitral stenosis the return to normal or near normal in about one-third of all cases operated on is remarkable.

TABLE XIII.—*Post-operative First Heart Sound*

First Heart Sound	Incidence	Functional Result		
		Excellent	Good	Fair or Poor
Intensity diminished by 2 or 3 grades. Now grade 1 or normal	30%	81·5%	18·5%	—
Intensity slightly diminished. Now grade 1 or 2	25%	30%	61%	9%
Unchanged	22%	20%	50%	30%
Now soft or normal due to mitral incompetence	23%	—	33·3%	66·6%

It is concluded that a loud first heart sound is excellent evidence of mitral stenosis, but gives little indication of its degree; its presence is a talisman against serious mitral incompetence.

Mitral Systolic Murmur

A loud mitral systolic murmur (grade 3 or 4) was heard in all the cases of pure mitral incompetence except two in which the murmur was only moderate in degree; a thrill accompanied the murmur in 43%. A similar loud murmur was also heard in all the cases of combined mitral stenosis and incompetence in the medical group except two in which it was also only moderate in degree; a thrill accompanied this murmur in 14%. No case of significant mitral incompetence without a systolic murmur of at least moderate degree was encountered in the whole series. In the surgical group there were naturally far fewer cases of significant mitral incompetence: here a loud mitral systolic murmur was heard in 11.4%, a moderate murmur in 9.3%, a faint murmur in 8.6%, and no mitral systolic murmur at all in 66.4%; in 4.3% of cases a tricuspid systolic murmur extending far out to the left was mistaken for a mitral murmur by some observers.

When the surgical cases were analysed in respect of the mitral systolic murmur there was close correlation between the incidence and grading of the murmur and the presence and degree of mitral incompetence recognized by the surgeon by direct palpation of the valve (Table XIV). For example, when there was no mitral systolic murmur there was no incompetence at all in 98% of cases; on the other hand, when the murmur was loud mitral incompetence was found in 88%, considerable in 58%, and mild or moderate in 30%. It can no longer be seriously maintained that a mitral systolic murmur is of little value in determining the presence or absence of mitral incompetence.

TABLE XIV.—*Mitral Systolic Murmur (Surgical Cases Only)*

Mitral Systolic Murmur	Grade of Mitral Incompetence			
	0	1	2	3
Absent	98%	2%	—	—
Grade 1	42%	42%	16%	—
„ 2	15%	70%	15%	—
„ 3 or 4	12%	18%	12%	58%

The effect of valvotomy on the mitral systolic murmur was recorded in all the surgical cases and has been correlated with the functional results (Table XV). As would be expected, the development of a loud mitral systolic murmur (grade 3 or 4) was associated with an important degree of mitral incompetence in the great majority of cases in which it occurred (84%). The functional result was relatively poor in this group. Those cases with a loud systolic murmur before the operation nearly always had a loud murmur afterwards and did not do well, 90% of them being classed as fair or poor and none as excellent. Apart from these two groups the functional result was much the same whether a grade 1 or grade 2 mitral systolic murmur developed, whether such a murmur present before the operation diminished or even disappeared (which was rare), whether a grade 1 or grade 2 systolic murmur remained unchanged, or whether there was no murmur before or afterwards. As many as 41% of the whole surgical group had no mitral systolic murmur before or after the operation, and 55% of those without a pre-operative murmur did not develop one afterwards; since the functional result was excellent or good in 85% of such cases it is clear that mitral valvotomy is capable of restoring excellent valve function. Relatively few (14%) of those without a mitral systolic murmur before the operation developed a grade 3 or 4 murmur afterwards, and all but two of them then had other evidence of serious mitral incompetence.

TABLE XV.—*Post-operative Mitral Systolic Murmur*

Mitral Systolic Murmur	Incidence	Functional Result			
		Excellent	Good	Fair	Poor
Grade 3 or 4 before and after	9%	—	10%	30%	60%
Increased to Grade 3 or 4	22%	4%	29%	38%	29%
Increased slightly to Grade 1 or 2	21%	53%	39%	4%	4%
No change Grade 0 to 2	41%	46·5%	38%	11%	4·5%
Diminished slightly	3·5%	50%	37·5%	12·5%	—
„ greatly	3·5%				

The Pulmonary Second Sound

By the pulmonary second sound is meant the second or pulmonary element of the second heart sound; it is rarely heard beyond the pulmonary area. When the second sound seems single, splitting can nearly always be recognized

during rather deep inspiration. It was necessary to appreciate the split before the pulmonary element could be properly analysed. Table XVI shows the relationship between the intensity of this pulmonary second sound and the pulmonary vascular resistance. The correlation is not as close as might be expected, but cannot be ignored: thus

TABLE XVI.—*Pulmonary Element of Second Sound*

Pulmonary 2nd Sound	Resistance		
	<6 Units	6–10 Units	>10 Units
Normal	91%	8%	1%
Accentuated Grade 1	76%	16%	8%
" " 2	42%	31%	26%
" " 3 or 4	33%	33%	33%

when the pulmonary second sound was normal the resistance was relatively normal in 81%; on the other hand, when the pulmonary element was markedly accentuated (grade 3 or 4) the pulmonary vascular resistance was high in 66%. Further details may be studied in the table. Closer correlation might well have been obtained if the second sound had been auscultated while the pulmonary artery pressure was being recorded, but this was impracticable.

It is concluded that the pulmonary element of the second heart sound is an important but not infallible guide to the degree of pulmonary hypertension present in mitral stenosis.

Pulmonary incompetence was recognized in 10% of the surgical cases, but in only 1% of the medical and in none of the cases of pure mitral incompetence. It was associated with an extremely high pulmonary vascular resistance in 55%, and with a high resistance (6 to 9 units) in the other 45%; it was never encountered when the resistance was under six units. The pulmonary artery was conspicuously dilated in nearly all these cases, the average degree of enlargement working out at just over grade 3.

The Mitral Opening Snap

This occurred in none of the group with pure mitral incompetence, but this only means that if a snap was present pure mitral incompetence was never diagnosed. There was, however, ample collateral evidence supporting this attitude.

Of the surgical cases 16.5% did not have an opening snap, excluding four cases which were put up for surgical repair of mitral incompetence. The absence of a snap was attributed to the following factors: (1) associated significant mitral incompetence without calcification (four cases); (2) associated significant mitral incompetence with heavy calcification (9 cases); (3) heavy calcification with trivial mitral incompetence (4 cases); (4) an extremely high pulmonary vascular resistance over 10 units (5 cases); (5) massive left atrial thrombosis (1 case); and (6) moderate aortic valve disease (1 case).

It is uncertain whether the explanation in these last two instances is correct. Since the opening snap is certainly due to the abrupt backward billowing of the mitral cusps, particularly the aortic, when the pressure within the left ventricle sinks rapidly below that in the left atrium at the end of the period of isometric relaxation, it is suggested that aortic reflux may prevent the snap by interfering with the backward movement of the aortic cusp.

Mitral incompetence of sufficient degree prevents the snap because in these cases there is far more destruction and rigidity of the mitral cusps than in pure stenosis, so that the rigging is disorganized and, if one thinks of the cusps as sails, they are too matted down to flap back as the pressure gradient is reversed. It may also be true that with sufficient incompetence the lack of obstruction at the mitral orifice itself prevents the snap by allowing free filling of the ventricle as in normal hearts.

It has been suggested that mitral calcification may be responsible for the absence of a snap (Wynn, 1953), and the findings here confirm this view. Conspicuous calcification is rare in the absence of incompetence, but it has occurred, and in addition to the four cases mentioned above two others have been seen recently both without a snap. Extreme rigidity of the cusps is assumed to be responsible. Of 13 additional surgical cases in which calcification was slight and in which there was no mitral incompetence, all had an opening snap.

An extremely high pulmonary vascular resistance obscured the snap in one-quarter of all such cases. Since the left atrial pressure was at a level which would certainly have been associated with a snap in uncomplicated cases of mitral stenosis, its relative lowering cannot be held responsible for the absence of the sign; moreover, the sign was in fact present in three-quarters of such cases, and was sometimes very loud. It is suggested that the snap may be masked by the very large pulmonary artery overlying the root of the aorta, so that sounds produced by the aortic cusp of the mitral valve are not readily heard at the base; also by a grossly distended right ventricle forming the apex of the heart, so that sounds transmitted through the left ventricle may be difficult to hear at the "mitral area." In one or two instances of extreme pulmonary hypertension the snap was recorded phonocardiographically when it could not be heard clinically; this was never so when a snap could not be heard in cases of mitral incompetence.

Amongst the 150 surgical cases there were only two instances of simple stenosis in which a snap was not recorded clinically. One of these had the largest mitral orifice in the series; in the other an error was suspected. Mitral valvotomy resulted in loss of the snap in 32% of the cases: half of these were associated with excellent results, the other half with the development of serious mitral incompetence.

In the medical cases an opening snap was not heard in 38%. The explanations were much as described for the surgical group, in that 16 had serious mitral incompetence without calcium, 10 had serious mitral incompetence with conspicuous calcification, one had conspicuous calcification without mitral incompetence, three had an extreme pulmonary vascular resistance, and one had moderate aortic valve disease. In addition, however, there were five cases in which the absence of a snap was attributed to the mildness of the lesion; in fact, 38% of really mild cases had no snap. It must be understood that in these the degree of stenosis approached the trivial. In relatively mild cases, in the sense that they were not severe enough to warrant valvotomy although otherwise quite well developed, a snap was always present. In the medical group also there was one case with predominant tricuspid stenosis in which a mitral opening snap could not be heard, and there was one instance in which failure to record a snap was believed to be a clinical error.

It is concluded that the opening snap is one of the most important signs of dominant mitral stenosis, and, like a loud first heart sound, is an excellent talisman against the presence of serious mitral incompetence. Although it signifies properly developed stenosis, being absent in many trivial cases, it does not necessarily mean that the stenosis is severe enough to warrant valvotomy.

The Third Heart Sound

This was never heard in cases of pure stenosis as noted by Brigden and Leatham (1953). It was present in 85% of the cases of well-developed mitral incompetence (grades 2 to 4) and in 25% of cases of mild mitral incompetence. It was present in 74% of the medical cases in which a serious degree of incompetence complicated mitral stenosis, but in only 25% of the surgical cases of similar kind, probably because there was relatively more stenosis in this small group. Of the surgical cases with a third heart sound not one did excellently or even well; indeed, three-quarters of them died. A third sound was never heard when a trivial degree of incompetence complicated mitral stenosis.

The sound was closely correlated with a hyperdynamic left ventricle. Thus 78% of all cases having such a left ventricular action without aortic incompetence had a third heart sound; conversely, 95% of cases with a third heart sound had a hyperdynamic left ventricle. This could be recognized both clinically and radiologically. The third heart sound, of course, is attributed to rapid filling of the left ventricle. The third sound was very closely correlated with the presence of a loud mitral systolic murmur; indeed, it was never heard without such a murmur. In fact, it was closely correlated with all the other signs of mitral incompetence as discussed elsewhere.

The difference between an opening snap and a third sound is usually obvious when both are classical, the opening snap being closer to the second sound, shorter, sharper, and higher-pitched in quality, and being very well heard at the left sternal edge; whereas a third heart sound is later, longer in duration, dull, relatively low-pitched, and best heard over the left ventricle at the apex of the heart. Again, the snap is well heard on expiration, whereas the third heart sound usually comes out better on inspiration. Unfortunately, the character of the third sound may become much more like an opening snap in advanced mitral incompetence in the sense that it may be less delayed and much sharper and higher pitched in quality than usual. The classical description of the third sound is based on its occurrence in normal individuals, usually children, and in association with heart failure (left ventricular diastolic gallop). In mitral incompetence the left ventricle fills more rapidly than in these conditions, and this is probably responsible for the modification of the sound.

When present before the operation, the third sound never disappeared afterwards; on the contrary, it was always louder. In the cases with combined stenosis and incompetence without a third sound pre-operatively, 85% developed the sound after valvotomy. In other words, relief of stenosis accentuated the signs of incompetence. In cases operated on for mitral stenosis with a trivial degree of incompetence, as many as 60% developed a third heart sound after valvotomy, although these patients often did very well functionally, the incompetence being only of moderate degree. A third sound associated with mitral incompetence also developed after valvotomy in 7.5% of cases without previous incompetence at all.

It is concluded that the presence of a third heart sound is excellent evidence of at least moderate mitral incompetence. Its presence offers a strong reason for not recommending valvotomy even in those rare instances in which a clinical opening snap is heard in addition to the third sound.

Mitral Diastolic Murmur

Particular attention was paid to the length as well as to the intensity of a mitral diastolic murmur, and whether or not it was accompanied by a thrill; both length and intensity were graded. By grade 4 length is meant that no gap could be detected between the murmur and the first heart sound, or between a diastolic murmur and presystolic accentuation; a grade 3 murmur means that a gap could just be recognized; a grade 2 murmur was of moderate length, and grade 1 very short. When there was tachycardia the heart was slowed by means of carotid sinus compression in order to grade the length of a murmur. When there was auricular fibrillation the length of the bruit was gauged during the longer pauses; sometimes these had to be induced by carotid sinus pressure.

The mitral diastolic murmur was long (grade 3 or 4 in equal proportion) in 85% of the surgical cases. In 15% only was it relatively short; one-third of these had an extremely high pulmonary vascular resistance (abolishing the murmur altogether in one instance); one-third had significant mitral incompetence; no explanation could be found in the remainder (5% of the whole series). An extremely high pulmonary vascular resistance also abolished the murmur in one of the medical cases.

In the group with almost pure mitral incompetence the murmur was very short in 48% and only moderate in length (grade 2) in 24%. It was never long, and was absent altogether in 28%. Moreover, when a diastolic murmur was present in mitral incompetence a third heart sound could nearly always be heard.

A mitral diastolic thrill was appreciated in 38% of the surgical group, in 29% of the medical, and in 20% of the cases with mitral incompetence. An attempt was made to find some factor which might favour the development of a thrill, but with little success. In the cases with a thrill valve calcification was present in 29%, against 28% in the group as a whole; the left atrial pressure averaged 21.4 mm. Hg, the cardiac output 3.95 litres a minute, and the pulmonary vascular resistance 5.1 units, against respective control figures of 22.5, 3.8, and 6.5; the mitral orifice was less stenosed than usual in 22%, average in 46%, tighter than usual in 22%, and extremely stenosed in 10%, against control figures of 9%, 48%, 17%, and 26% respectively, omitting cases with significant mitral incompetence. As a rule, the cusps were mobile in cases with a thrill; a tough fibrous orifice was present in 27%: these anatomical findings were much the same in the series as a whole.

It will be discerned that the only points of difference between cases with a diastolic thrill and the surgical group as a whole were that the pulmonary vascular resistance was a little lower, and that the incidence of cases with extreme and relatively mild stenosis was reversed. On looking into the resistance more closely it was found that an extreme resistance was present less than half as frequently in those with thrills as in those without. This was confirmed by an analysis of the medical group, in which none of the few with an extreme resistance had a thrill. This damping effect probably explained the relatively few cases of an extremely stenosed orifice amongst the cases with thrill referred to above.

The intensity of the mitral diastolic murmur has not been analysed separately, for the loudest murmurs were usually associated with a thrill, soft murmurs never.

[*Part II, with a list of references, will appear in our next issue.*]

Scientific Film Review for March, 1954, includes descriptions of eight new medical films. "Analysis of the Effect of Vasoactive Substances on the Blood Vessels in the Mesorchium of the Rat" (Ciba Laboratories) is described as a superb example of cinemicrography. Although intended for pharmacologists and physiologists, it is also suitable for medical societies. "The Children's Vocabulary of the New Sign Language" (Department of Phonetics, University College, London) demonstrates some 330 moving signs in Sir Richard Paget's new sign language. It is intended for teachers of the deaf and otologists. "Cold Agglutination of Human Blood" (Ciba Laboratories), partly in colour, is for haematologists and physiologists. "The Cyto-diagnosis of Uterine Cancer" (Ciba) is a useful colour film dealing with the recovery of vaginal contents, the technique of Papanicolaou's staining procedure, and the appearance of cancerous cells. The first part is primarily of value to gynaecologists and the remainder to pathologists and laboratory technicians. "Lymph Vessel Movement Studies in the Mesentery of the Rat" (Ciba) is meant for pharmacologists and physiologists. "Nalorphine" (Wellcome Film Unit) demonstrates the antagonistic action of this drug to morphine, methadone, and thiambutene. "A New Approach to the Surgery of Peptic Ulcer" (Allen and Hanbury) is a demonstration in colour of the difference between Billroth partial gastrectomies and the jejunal replacement technique, with particular emphasis on the latter. It is likely to be of special interest to gastric surgeons and surgical societies. "Nydrazid in the Treatment of Tuberculosis" (E. R. Squibb and Sons) is a coloured film intended for chest physicians, tuberculosis officers, etc.

THE SURGICAL TREATMENT OF PECTUS EXCAVATUM (FUNNEL CHEST)

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Pectus excavatum is a depression deformity of the anterior chest wall that has been recognized under a number of names: funnel chest, trichterbrust, chonechondrosternon, koilosternia, and others. Despite the considerable literature on this well-known entity many differences exist concerning its development and management. A brief review of the current concepts and the results of surgical treatment used in this unit are presented.

Aetiology

The exact aetiology is still uncertain. Of the many theories advanced none could serve as a fit basis of treatment until Brown (1939) demonstrated that the deformity was due to a short central tendon of the diaphragm. Brodkin (1951) observed a diminished inspiratory sternal retraction on the homolateral side following procaine injection of the phrenic nerve. We have noticed an almost complete disappearance of inspiratory sternal retraction when the diaphragm has been paralysed by curare. It does seem likely that some congenital abnormality of the diaphragm is primarily responsible for the condition.

The deformity is noticed shortly after birth, but in some individuals it may not become apparent until later years, and it may be observed by the parents for the first time in early adolescence. That there is a strong genetic factor is well shown by the commonly reported occurrence of multiple cases within a single family and in lineal descent through several generations (Sainsbury, 1947). This has been confirmed in our series. It is characterized by a progressive posterior sternal depression and distortion of the adjacent costal cartilages that begins near the sterno-manubrial junction and reaches its deepest point at the xiphoid. In infancy this retraction may be apparent only with deep inspiration and is best seen when the child is crying, a severe degree of deformity then being produced which immediately corrects itself after the inspiratory effort is over. Unfortunately it often tends to progress to a permanent bony deformity, and there is no way of knowing in which individual this will occur. In one of our cases it progressed from a mobile deformity seen only on deep inspiration to a fixed deformity in a period of six months. The deformity is often symmetrical but not always so. In time a characteristic posture develops. The ribs acquire a lateral flare and the chest becomes flattened and pulled down upon the abdomen, a dorsal kyphosis develops, and the head tends to protrude forward. The appearance is that of a thin round-shouldered, hollow-chested, pot-bellied individual. The costal cartilages dip into the sternum at a steep angle and the xiphoid is often impalpable from the overcrowding of the sixth and seventh cartilages. The depression, which is often extreme, usually deepens on inspiration.

The thoracic viscera may be affected by compression and distortion. Although there is interference with respiration this is seldom at a critical level, and in many instances the commonly used clinical tests of respiratory function may fail to show any serious alterations. There is adequate evidence in the literature to show that symptomatic cardiac disturbances are not uncommon. Electrocardiograms, angiocardiograms, and cardiac catheterization have provided convincing evidence of disturbed cardiac function. Symptoms of tachycardia, palpitation, arrhythmia, and dyspnoea can occur at an early age. A systolic murmur may be heard, and on the basis of this some of these children have been labelled "heart disease" and precluded from many activities at school.

The purpose of surgical treatment is to correct the sternal and costal cartilage deformity. This is of no value unless persistent post-operative supervision is carried out to see that the patient corrects the kyphosis, which is, of course, secondary to the diaphragmatic and sternal abnormality. The younger the patient the easier this is, and we are reluctant to operate on patients over 20 unless they have symptoms. There is no doubt that these symptoms will be relieved in this older age group, but the bad posture will probably persist.

Infants under the age of 6 months should not have treatment, as inspiratory sucking-in of the sternum may be present in the newborn and gradually disappear during the first few months of life. Delay in treatment is to be condemned, because in the early stage, when the chest wall is still mobile and deformity is produced only on deep inspiration, the operation is a relatively minor one. When the sternum has become detracted down and the costal cartilages are permanently deformed then a more extensive procedure is necessary. Excluding those who are too old and too young, we feel that all cases should have surgery.

It is striking how the patients' and their parents' concern over this disability is masked. When first seen in the out-patient department and accepted for operation their true feelings become more apparent, though restrained. It is only after operation that their real feelings are manifest. There is a reluctance on their part to believe that surgery can offer anything because they have been repeatedly told that nothing can be done. Many of them have had prolonged treatment in physiotherapy out-patient departments with little or no improvement, and an attitude of *laissez faire* exists. These children are often very conscious of their defect. They are shy of their complaint; boys frequently undergo teasing at school and girls feel handicapped, particularly as they reach adolescence. It has impressed us in their first follow-up how they volunteer a sense of well-being and an improved exercise tolerance. This latter is very constant. The patient often states that he can now do far more than he did before and that he can keep up with boys of his age effortlessly, whereas prior to the correction of his pectus he had found difficulty in keeping up. Thus surgery is undertaken: (1) for cosmetic reasons; the penalty for this is a scar which can be hidden, but it is impossible to hide the bad posture in a well-established case; and (2) to alleviate symptoms; these may be severe. It is true that the percentage of cases with symptoms in our series is not representative, as we are more inclined to see cases who have symptoms.

Brown (1939) and Ochsner and De Bakey (1939) put surgical treatment of pectus excavatum on a sound basis. Many modifications and variations have appeared since that time (Sweet, 1944, 1950; Ravitch, 1949; Wahren, 1950; Brodkin, 1951; Woods *et al.*, 1952; Johnson and Kirby, 1952). Techniques involving the use of plaster casts, various forms of external traction and fixation, grafts of bone and cartilage internally to support the sternum, and plastic operations upon the deformed costal cartilages are in current practice. It is understandable that such a state of confusion should exist, since the exact aetiology of the condition is not completely settled and no one method of treatment has been 100% successful.

Most present-day operations are based upon the principles of Brown. It is mainly in the method of maintaining sternal elevation and in dealing with the deformed costal cartilages that the various techniques differ. We have been impressed with the modification described by Ravitch (1949), and our present technique is based essentially upon this method. It requires no traction or added supports externally or internally.

Technique of the Operation

The anaesthetic consists of nitrous oxide, thiopentone, curare, and oxygen with an endotracheal tube. A midline incision is made from above the upper limit of the deformity to the epigastrium. The pectoral muscles are dissected laterally to expose the full length of the deformed costal cartilages. Because of the crowding and depression, the lowermost two costal cartilages on each side usually need to be resected to expose the xiphisternal junction. After dividing this a tough fibrous band may be seen running from the posterior rectus sheath to the back of the sternum. This is not always present. When this so-called substernal ligament is divided the xiphoid and rectus retract, sometimes with an audible snap. It is now possible to palpate the entire posterior surface of the sternum and to free all adhesions and remaining diaphragmatic attachments.

If the costal cartilages are deformed they must be completely removed to the level where the posterior angulation of the sternum begins (Fig. 1). The remaining intercostal structures are severed from the sternum, leaving it completely free except for its junction with the manubrium. At the site of angulation a transverse cuneiform osteotomy is made through the anterior cortical lamella of the sternum. In children an ordinary gouge is adequate; adults may require an osteotome. The sternum now may be bent sharply anteriorly to fracture the posterior cortical table. By means of two or three vertical mattress sutures the sternum can be maintained in a position of slight over-correction. The pectoral muscles are sutured to the periosteum of the anterior surface of the sternum near the midline and the wound is closed without drainage. A simple gauze dressing is used to cover the incision, and the patient is got up and dressed the following day. There has been no fixation in any case.

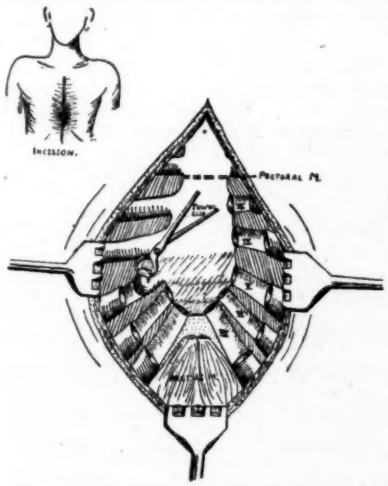

FIG. 1.—Diagram showing the third, fourth, fifth, sixth, and seventh cartilages removed on the left, and the fifth being enucleated on the right, leaving the posterior perichondrial layer intact. The xiphoid has been detached with the rectus after division of the substernal ligament. The upper line shows the usual site of the transverse osteotomy.

If the operation is done in infancy, before there is any fixed deformity of the sternum or the costal cartilages, only a small transverse incision is needed over the xiphisternum. The xiphisternum joint and the substernal ligament are divided and the sternum and the lowest costal cartilages are freed of any diaphragmatic attachments. We have abandoned subperichondrial resection of the costal cartilages, since it can be tedious and is felt to be unnecessary. A section of each side of the cartilage is freed from the intercostal insertions and a curved blunt periosteal elevator is inserted beneath the cartilage and elevated. This elevated cartilage is then easily divided with a knife and each end picked up in turn with a towel clip, stripped free, and removed. A narrow strip of posterior perichondrium is usually left. The chest becomes firm in two weeks.

In a case with fixed deformity it is essential to be radical. If the deformity of the third costal cartilage is present but not marked it is wrong to spare it. This mistake was made in Case 2; the cosmetic result has been spoilt by the overgrowth of this third cartilage and the patient has a mild degree of pectus carinatum.

The extent of the deformity in each individual must be carefully assessed clinically and at operation to ensure complete removal of all deformed costal cartilages. No harm follows accidental opening of the pleura with an endotracheal tube in place. The lung is kept inflated, the pleura is closed, and any small remaining pneumothorax is allowed to absorb. Occasionally fullness beneath the lower end of the incision will require aspiration, but routine drainage of this space has not been found to be necessary. Respiratory paradox of the anterior chest wall has not been a problem. It was seen in only one patient; she developed a lung infection two days after the operation and the paradox was rapidly brought under control by giving her four million units of penicillin a day. Diligent pre-operative and post-operative physiotherapy is most important in achieving a smooth convalescence and a good result.

The early results in this series of 10 patients is very satisfactory, the longest follow-up being 11 months. Concerning the question of later recurrence, we gain solace from the report of Ravitch (1951), whose patients, treated in this way, have been followed up for five and six years with no evidence of recurrence.

Case Reports

Full reports on all these cases are not given, as in many this would be repetitive; only cases with features of interest are discussed.

The age range of the patients was 2 to 17 years. There were seven males and three females.

Case 1.—A girl aged 15 had had severe symptoms for two years. She was afflicted by frequent attacks of giddiness, which were quite unrelated to any particular posture or movement. For 18 months she had noticed a persistent sense of constriction in the chest and on exercise experienced incapacitating discomfort along the subcostal margin, this being always associated with severe palpitations. At the end of a day at school her ankles were swollen. She had ceased all sporting activities because of pain and dyspnoea. On examination the typical deformity of a well-established funnel chest was seen (Fig. 2). Her kyphosis was not fixed,

FIG. 2 FIG. 3

FIG. 2.—Case 1. This patient presented with symptoms of pain, dyspnoea, giddiness, and palpitation. Severe degree of deformity and paradoxical movement on inspiration. FIG. 3.—Case 1. Follow-up 11 months post-operatively. Correction maintained and symptoms alleviated.

and there was marked paradoxical movement of the sternum on inspiration. *X*-ray examination showed a rotation of the heart into the left chest. Angiocardiogram revealed no filling defect. E.C.G. was normal and the circulation time using dehydrocholic acid was seven seconds. In July, 1952, the deformity was repaired. The result is shown in Fig. 3. At her last follow-up, 10 months after operation, there was no recurrence of deformity, her posture was excellent, and she had no disability.

Case 2.—A boy aged 5 had been subject to "bronchitis" all his life. The deformity was first noticed when he was 2½, and it had progressed since. In all respects he seemed a healthy boy except for his recurrent chest infections. On examination a well-marked deformity was seen. On inspiration there was a severe degree of paradoxical movement of the sternum. Repair was carried out. He had a well-formed substernal ligament, and when this was divided the xiphoid and recti sprang away. The mistake was made of not being radical enough; the third costal cartilage should have been removed on either side. His follow-up from the cosmetic point of view was disappointing in that there was some overgrowth of the third costal cartilage. There was no paradox, and since his operation nine months previously he had had no further attacks of bronchitis; this was the longest period he had been free of chest infection.

Case 3.—A boy aged 10½ was completely symptomless. His parents requested the operation because they were a Service family and were anxious for the boy to go ultimately into the Services. Also, they lived in a families camp and

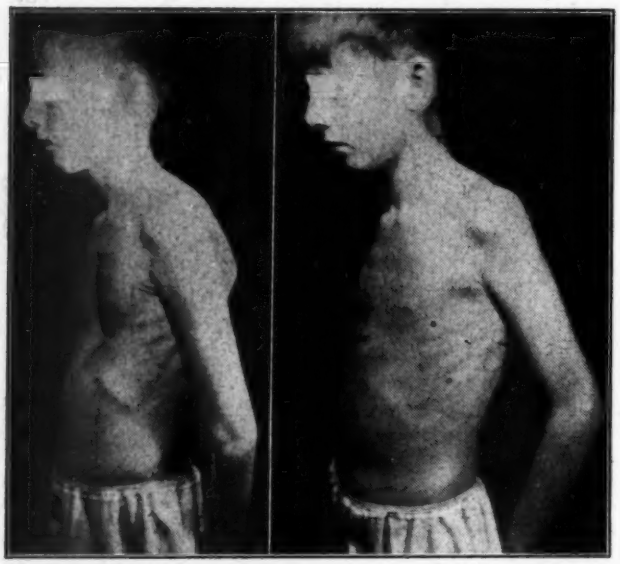

FIG. 4 FIG. 5

FIG. 4.—Case 3. This patient had no symptoms. FIG. 5.—Case 3. Photograph taken just before discharge.

had seen a previous case returned from the unit. Fig. 4 shows the degree of deformity. This boy had a marked paradox. Fig. 5 was taken immediately before his discharge and well illustrates the need for close supervision over the next three to five months.

Case 4.—A girl aged 13 complained of pain in the xiphisternal region associated with exercise. It was a sharp non-radiating pain. It had been present for one year. She became more breathless than her friends and at times found it difficult to keep up with them. Because of a murmur in her heart the school doctor had years previously told her that she had heart trouble. Examination showed typical funnel-chest deformity. There was a systolic murmur over the mitral area. The deformity was repaired; the murmur has now disappeared, and she indulges in full activities without any discomfort.

[Since this paper was submitted five additional cases have been repaired. They have all done well and no complications have arisen.]

Summary

The current concepts of pectus excavatum are briefly reviewed.

A prophylactic operation is advised at an early age to prevent a progressive and permanent deformity. The two main indications for surgery are cosmetic and symptomatic. The technique employed requires no external traction or added internal support. In infancy the dividing of the xiphisternal joint and freeing of the sternum from the diaphragm correct the deformity. Older subjects require the added resection of all deformed costal cartilages and a transverse wedge osteotomy of the sternum.

Ten patients treated by this method are presented. There were no deaths or complications. The early results are satisfactory and encouraging. It is necessary to be radical and to excise all the deformed cartilages.

REFERENCES

Brodkin, H. A. (1951). *Dis. Chest*, 19, 288.
Brown, A. L. (1939). *J. thorac. Surg.*, 9, 164.
Johnson, J., and Kirby, C. K. (1952). *Surgery of the Chest*. Year Book Publishers, Chicago, Illinois.
Ochsner, A., and De Bakey, M. (1939). Ibid., 8, 469.
Ravitch, M. M. (1949). *Ann. Surg.*, 129, 529.
—— (1951). *Surgery*, 30, 178.
Sainsbury, H. S. K. (1947). *Lancet*, 2, 615.
Sweet, R. H. (1944). *Ann. Surg.*, 119, 922.
—— (1950). *Thoracic Surgery*. Saunders, Philadelphia and London.
Wahren, H. (1950). *Acta chir. scand.*, 99, 568.
Woods, F. M., Overholt, R. H., and Bolton, H. E. (1952). *Dis. Chest*, 22, 274.

ANTIHISTAMINE THERAPY

WITH SPECIAL REFERENCE TO SKIN DISORDERS

BY

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During the past five years a separate out-patient clinic has been held twice a month for the purpose of studying the administration and overall value of the antihistamine group of drugs. Most of the patients attending the clinic have had urticaria. The main problems connected with the use of these drugs can be dealt with under headings of administration, ill-effects, and skin disorders affected.

The Drugs Available

The following drugs of the group are available for oral use in this country.

Official Name	*Proprietary Name*
Antazoline	Antistin (Ciba)
"	Histotab (Boots)
"	Ben-a-Hist (Bencard)
Bromazine	Ambodryl (Parke, Davis)
Chlorcyclizine hydrochloride	Histantin (Burroughs Wellcome)
" "	Di-paralene (Abbott)
Diphenhydramine hydrochloride	Benadryl (Parke, Davis)
Mepyramine maleate	Anthisan (May & Baker)
Methaphenilene hydrochloride	Diatrin (Warner)
Phenindamine hydrogen tartrate	Theophorin (Roche)
Promethazine hydrochloride	Phenergan (May & Baker)
Tripelennamine hydrochloride	Pyribenzamine (Ciba)
Meclozine dihydrochloride	Ancolan (B.D.H.)
None	Actidil (Burroughs Wellcome)
None	Synopen (Geigy)

"Dibistin" (Ciba) is a mixture of antazoline and tripelennamine.

"Avomine" (M. & B.) and dimenhydrinate ("dramamine," Searle) contain antihistamines but are primarily used for travel sickness.

There is not much information available about the equieffective doses of the various drugs. In conjunction with Professor W. A. Bain, I carried out comparisons of various drugs in their effects on induced histamine weals in man. It was then found that for single doses 40 mg. of promethazine was equivalent to 275 mg. of mepyramine and 600 mg. of antazoline (Bain, 1949). With repeated doses the drugs with a long action, such as promethazine, will build up a greater effect; and after a week's therapy promethazine, 40 mg., was found to be equivalent to mepyramine, 560 mg., given in a 24-hour period.

The specific histamine antagonism is apparently the same with all the drugs, but the nature and degree of side-effects vary. It is the incidence of the latter, when equieffective doses of the drugs are compared, that usually determines which is the most suitable drug. In a clinical assessment (Bain, Hellier, and Warin, 1948) it was shown that the incidence of drowsiness was greater with diphenhydramine than with mepyramine. When promethazine given in a single dose at night was compared in this respect with mepyramine given three times a day, the side-effects were less, and most patients preferred promethazine (Bain, Broadbent, and Warin, 1949). Recently a similar comparison has been undertaken, using promethazine in a single dose at night and chlorcyclizine given twice a day. Forty-nine patients with persistent urticaria were treated with the drugs in turn, and the dose in each case was adjusted to a level giving approximately the same degree of reduction of the wealing. Nineteen patients had some side-effects with one or both drugs. In seven of these they were less or nil when on chlorcyclizine, in two they were less or nil on promethazine, and in 10 there was no difference. In this clinical comparison chlorcyclizine, 75 mg., gave approximately the same effect as promethazine, 25 mg.

From the preliminary tests it was shown that antazoline was a relatively weak antihistamine, and it has not been used in the clinical work. Tripelennamine has a similar structure to mepyramine and its effects are about the same.

Meclozine, phenindamine, and methaphenilene do not appear to have any useful advantage over the others, but, together with the recent additions, bromazine, "actidil," and "synopen," my experience with these drugs has been limited, and no clear comparison seems to be available.

In the clinic the main drug used has been chlorcyclizine, but a few patients have had promethazine or mepyramine, and in some cases diphenhydramine has been used when the additional sedative action has been required.

Practical Points in Administration

The dose of the drugs required to suppress weals varies greatly. Apart from the question of body weight and age it has been shown that individual patients vary considerably in the degree of histamine antagonism given by the same dose of one of the drugs (Bain *et al.*, 1948). Thus the same degree of histamine antagonism given in one patient by, for example, 300 mg. of mepyramine a day may be given in another by 900 mg. If a patient shows a small antihistamine effect with one drug of the series, a small effect will generally be given by the other drugs. In the practical administration of the drugs the variation in response is usually overcome by giving the patient an average dose, and if the symptoms are not controlled the dose is raised until either the desired effect is brought about or side-effects become too great.

In addition to this variation in individual response to the drugs the strength of stimulus evoking the treated disorder will vary from patient to patient. If the tendency to urticaria is very great even in a patient relatively sensitive to the antihistamine, it may be impossible to reach a high enough dose of the drug to control the eruption. This is more often seen in the acute attacks of urticaria.

The strength of the stimulus may also fluctuate in the same patient. For example, urticarial weals satisfactorily suppressed by certain doses of an antihistamine may suddenly reappear coincident with additional psychological stress, or other factor. In such a case higher doses of the drug may again suppress the weals (Warin, 1950a).

Judged by the response of the induced histamine weal, children are relatively insensitive to antihistamines, and consequently a larger amount than the usual proportional age reduction of the dose is necessary to get an effect on weal formation.

The frequency of administration will vary with the length of action of the drugs: promethazine has a long action, and if given in a single dose may control the urticaria throughout the 24 hours. However, in some patients on a single dose the weals return towards the end of the 24-hour period. This could, of course, be controlled by giving a second dose, but can also often be controlled by increasing the single nightly dose. Chlorcyclizine is relatively long-lasting and it seems satisfactory to give the drug twice a day. With mepyramine it is usually necessary to give the dose three or four times a day.

Chronic urticaria quite often fluctuates regularly throughout the 24-hour period, appearing or becoming worse in the evening or in the early hours of the morning. When this is so the drugs should obviously be given to allow the maximum antihistamine effect at this time. The time taken from ingestion to full effect is about two to four hours with most of the drugs. Therefore, for example, in a patient who has a persistent slight wealing but exacerbations in the late evening, the best method of administration might be to use chlorcyclizine, 50 mg. in the morning and 100 mg. at tea-time. In a patient requiring large doses of an antihistamine one may be able to avoid unpleasant side-effects at work or during the daytime by so adjusting the times of administration.

The antihistamine drugs vary in the rapidity of onset of action after ingestion. The new drug actidil apparently reaches its maximum effect more quickly than the others, and it may prove to be the drug of choice when a rapid effect is required.

Often the type of patient who suffers from a persistent urticaria does not sleep well, quite apart from any itching, and in these cases it may be worth while giving at night one of the antihistamine drugs, which usually produces a drowsy effect. Diphenhydramine and promethazine are perhaps the best for this purpose, and, indeed, recently they have been used deliberately as mild sedatives. The drugs can be mixed, and a quite useful combination is chlorcyclizine, 50 mg. twice daily, with diphenhydramine, 50 mg. at night.

The dose should always be gradually reduced before discontinuing treatment. Otherwise, if the tendency to urticaria remains unchanged, the patient may find a sudden and full return of the rash very distressing.

Sometimes the conditions treated are periodic, with intervals of a few weeks between attacks, and in these cases it may be as well to start off with a period of regular daily administration, but later on it is often satisfactory to give the patient a supply of the tablets to take for a few days as soon as the attack begins.

Ill-effects of Antihistamines

The main side-effect of the antihistamines is drowsiness. As has been discussed, this is commoner with some drugs, and is, of course, more often encountered when large doses are employed. It is very difficult to assess the overall incidence of drowsiness. On direct questioning practically all intelligent sensitive patients having average doses will have noticed a little drowsiness. The danger of drivers and workmen in hazardous occupations taking the drugs is of course present, but has probably been overemphasized. Under such circumstances the first dose should, if possible, be taken at a week-end or, if more urgent, in the evening after returning home. In the clinic a number of public transport drivers and a motor-cycle "speedway" rider have been treated for long periods.

Many other side-effects have been described; these include dryness of the mouth, headache, blurred vision, dysuria, nightmares, depression, and other mental changes.

A curious effect is that of a twitching sensation, which is usually felt more in the legs. The muscles ache and the patient is constantly moving and stretching the limbs. Restlessness and a desire to get up and walk about are often felt. This side-effect was first noticed with promethazine (Warin, 1950b), but during the past two years it has been noted with chlorcyclizine and also with diphenhydramine. The symptoms may not be described by the patient, but are not uncommon if specifically inquired about.

Mepyramine and tripelennamine sometimes give rise to nausea, vomiting, abdominal colic, and diarrhoea. These side-effects are uncommon if it is remembered to give the drugs with or after meals. In potential epileptics the drugs occasionally produce fits (Churchill and Gammon, 1949).

Death associated with convulsions has been recorded in 14 cases when large overdoses have been swallowed accidently by children. In only one of these children did the amount taken approach the therapeutic dose. This occurred in a child aged 14 months who died after accidentally taking mepyramine tablets, the dose of which was unknown, but assessed at 2–300 mg. (Prain, 1950).

Wyngaarden and Seevers (1951) mention reports of three cases of haemolytic anaemia and nine cases of agranulocytosis. In one of the latter the patient, who had mepyramine for three months, died (Glassmire, 1951). Bénard and others (1947) report the case of a patient who died with jaundice and anaemia, but this did not appear to be definitely related to the small dose of "antergan" administered.

Considering the vast amount of the drugs used throughout the world, these few cases have little significance, and it seems that in general these substances are relatively free from serious toxic effects in therapeutic doses, even when administered for prolonged periods. Some patients in the clinic have now received regular and continuous treatment for three to four years without any deleterious effects. There is no definite evidence that tolerance to the antihistamine effect of the drugs occurs. Certainly the drowsy side-effects often become less after a few days and patients may think that they are becoming tolerant to the drugs. It is also possible that the tendency to urticaria becomes greater and gives rise to an increase in weals in a patient in whom the rash was previously reduced, so creating an impression that tolerance was developing. However, the degree of reduction of the induced histamine weal after many months' treatment is unaltered (Warin, 1948).

Skin Disorders Affected

Acute chronic and papular urticaria, dermatographism, and the urticarial response from stings and bites can all be affected. The weals may be completely suppressed or they may just be reduced in number and size according to the level of antihistamine effect obtained. If the underlying stimulus to the urticarial reaction is considerable, as may occur with drug or food urticaria, or if the patient is relatively resistant to the drugs, as, for example, in children with papular urticaria, the weals may not be obviously affected by the doses commonly prescribed.

Although it is not intended here to discuss in detail the clinical value of suppressing or reducing the weals in urticaria, the main conclusions might be mentioned. When the attack is self-limited, as in acute or recurrent urticaria, symptomatic relief with the drugs will have an obvious place in treatment. In chronic urticaria the weals are reduced or suppressed only so long as the drugs are given, and treatment may have to be continued for many months. The period that the underlying tendency to wealing lasts is probably neither shortened nor prolonged by such treatment, but as in most cases considerable relief is obtained it is thought that antihistamine treatment has an important place in the management of these cases.

It is very difficult to decide how much giant urticarial swellings are affected by antihistamines. In such giant urticaria (angioneurotic oedema or Quincke's oedema) the oedema is largely in the subcutaneous tissues. These swellings may or may not occur in association with chronic urticaria. Clearly they do not respond to antihistamines as well as the ordinary dermal weals, and when both conditions are present the dermal weals can often be completely suppressed while giant swellings may still occur. Fifty-two cases with recurrent giant swellings have been treated, and, although it is very difficult to institute adequate controls in a condition with such irregular manifestations, 40 patients have had a reduction in the number and size of swellings when on antihistamines. Furthermore, there was usually a reduction in the severity and length of time the swellings were present if the drugs were given only at the earliest possible stage in an attack. It therefore seems that, although not affected as much as dermal weals, subcutaneous swellings are reduced.

A type of wealing may occur in association with certain other eruptions, including dermatitis herpetiformis, erythema multiforme, and actinic prurigo. An attempt to assess the effect of antihistamines on these conditions has been made, the antihistamine effect being checked by noting the reduction of induced histamine weals and using a mild sedative in the control periods (Warin, 1950a). In 10 cases of dermatitis herpetiformis it was concluded that, although one or two patients appeared to be improved, in general no specific action on this condition could be demonstrated. Since then a number of cases have been treated, and it has appeared that the cases benefited have been those in which the weal element of the rash has been a prominent feature. Ten cases of actinic prurigo were also assessed in a similar manner: although conclusions were not definite there was apparently some effect from antihistamines. It has proved very difficult to decide whether or not erythema multiforme lesions are reduced.

The eczematous dermatitis reaction affects the epidermis chiefly, but in some cases the skin is raised and tense owing to an associated dermal oedema. In my experience it is only this latter type of the eczematous dermatitis reaction which is affected, and then only with regard to the dermal oedema. The drugs have been used to reduce pruritus from various causes, but it is only the type associated with wealing, as in urticaria, that can regularly be affected.

From time to time it has been claimed that certain other eruptions are affected by the drugs, but as experience becomes wider the number of conditions benefited becomes smaller and it may well be shown eventually that the only conditions affected are those in which wealing is part of the eruption. Halpern (1952) has suggested that the main effect of antihistaminic substances is on the neuromuscular mechanism of certain small vessels. As wealing is dependent on the dilatation of small vessels in the dermis, it would seem likely that the main action of the drugs is to antagonize the dilatory action of histamine on the dermal vessels and to a less extent on the subcutaneous vessels.

Summary

The antihistamine drugs available in this country are listed and compared.

Certain practical points in administration of the drugs are mentioned.

Ill-effects of the drugs are discussed.

The skin disorders affected are discussed, and it would seem possible that the only conditions of the skin which are benefited by antihistamines are those in which wealing is part of the eruption.

I would like to express my thanks to Dr. C. D. Evans for so kindly referring many patients to me.

REFERENCES

Bain, W. A. (1949). *Proc. roy. Soc. Med.*, **42**, 615.
—— Broadbent, J. L., and Warin, R. P. (1949). *Lancet*, **2**, 47.
—— Hellier, F. F., and Warin, R. P. (1948). Ibid., **2**, 964.
Bénard, H., Rambert, P., Tissier, M., and Scherrer, J. (1947). *Paris méd.*, **37**, 9.
Churchill, J. A., and Gammon, G. D. (1949). *J. Amer. med. Ass.*, **141**, 18.
Glassmire, C. R. (1951). *J. Maine med. Ass.*, **42**, 83.
Halpern, B. W. (1952). Paper read at a meeting of the British Association of Allergists, February, 1952.
Prain, J. H. (1950). *British Medical Journal*, **1**, 1375.
Warin, R. P. (1948). Ibid., **2**, 169.
—— (1950a). *Brit. J. Derm.*, **62**, 159.
—— (1950b). *Bristol med.-chir. J.*, **67**, 77.
Wyngaarden, J. B., and Seevers, M. H. (1951). *J. Amer. med. Ass.*, **145**, 277.

INCIDENCE OF ALLERGIC DISEASES IN GENERAL PRACTICE

BY

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The symptoms of allergic disorders depend upon the antigen-antibody reaction in the shock organ. Von Pirquet defined allergy as an "acquired specific altered capacity to react." Even after 50 years of research in this field, Pepys (1953) points out that this statement is still valid.

The findings of a collagen lesion in serum sickness, periarteritis nodosa, lupus erythematosus, and rheumatic fever, and the improvement in these conditions after cortisone or A.C.T.H. therapy, suggest that allergic reactions might play some part in their aetiology. We decided to investigate the incidence of five of the common allergic diseases in our practice—namely, bronchial asthma, allergic rhinitis, urticaria, atopic eczema, and drug allergy.

The practice, an industrial one comprising about 4,000 patients, is carried on from two surgeries. Details of attendances and treatment are recorded daily in each surgery. The period of this investigation was from September 1, 1952, to September 1, 1953.

Diagnosis of the Allergic Diseases

Only a brief account of the diagnosis and differential diagnosis of allergic diseases is given.

The general practitioner has the best opportunity of diagnosing common allergic diseases. A careful history-taking is most important, and should include the main complaints, details relating to the cause of illness, past medical history, family and social history, environmental background, and history of previous treatment. History-taking has been emphasized by Tuft (1949), Herxheimer (1952), Sheldon *et al.* (1953), and other allergists. The therapeutic application of adrenaline and ephedrine in acute attacks of asthma and antihistamines in allergic rhinitis and urticaria is helpful in establishing the diagnosis.

We agree with Freeman (1950) that *x*-ray examination of the chest in asthma is not essential. Laboratory investigations, skin tests, and estimations of vital capacity are more useful for the management of the patients than for diagnosis. Cases of chronic bronchitis and emphysema were excluded.

In allergic rhinitis a history of recurrent attacks of rhinorrhoea, sneezing, itching in the eyes, nose, and pharynx, and a general feeling of fatigue are the complaints. Examination reveals bluish oedema of the nasal mucosa and sometimes polypi. Sheldon *et al.* point out that sore throat and enlargement of cervical lymph nodes are not common in allergic rhinitis. The finding of large numbers of eosinophils in nasal smears helps in doubtful cases.

Urticaria may be acute or chronic : the acute type generally disappears within a few days or weeks; chronic urticaria may continue for months or years (Tuft, 1949; Sheldon *et al.*, 1953). The patient complains of an itching or burning sensation. The diagnosis is made on the finding of weals, which may vary in size and shape.

Atopic eczema was diagnosed by the finding of superficial cutaneous eruptions involving the flexural surfaces; adequate history is very important (Vickers, 1952; Sheldon *et al.*, 1953).

Drug allergy presents a great problem. A memorandum on the sensitivity of antibiotics (*Med. Offr*, 1953) emphasizes the importance of this subject. Reports of deaths attributed to phenylbutazone have appeared in the medical and lay press. Penicillin may cause dangerous or even fatal reactions (Pick and Patterson, 1953; Siegal *et al.*, 1953). Drug allergy may develop after ingestion, parenteral injections, or contact with the offending agent, and it may manifest itself in the immediate or delayed type of reaction (Rackemann, 1953; Pepys, 1953; Sheldon *et al.*, 1953). The manifestations of drug allergy are various, the commonest being the skin lesions. The most serious, however, are agranulocytosis and thrombocytopenia, and thiouracil is the common cause of the former and "sedormid" (Grant, 1953) of the latter. Diagnosis depends on history, general examination, and cessation of symptoms on stopping the offending drug.

Differential Diagnosis

The diagnosis of straightforward cases of allergic disease, like many other medical or surgical conditions, is not difficult. The elderly hypertensive and arteriosclerotic patient with incipient cardiac failure gets attacks of dyspnoea; the child with recurrent attacks of bronchitis and bronchiolitis presents wheezing and cough. Periarteritis nodosa or Löffler's syndrome (Rubin, 1947) brings on asthma-like attacks. Here the eosinophil count is of great value. Bronchogenic carcinoma is getting common, and we encountered one patient suffering from it who self-diagnosed asthma.

Septal deflections, enlarged turbinates, enlarged tonsils and adenoids, infective sinusitis, and the common cold are the conditions mistaken for allergic rhinitis.

Children like to scratch the itchy urticaria weals; urticaria should then be differentiated from scabies or chickenpox.

In atopic eczema the secondary changes resulting from scratching and infection may lead to a variety of skin abnormalities : erythema, papules, wealing, scaling, pigmentation, and lichenification. Cases of seborrhoeic dermatitis and contact dermatitis were excluded.

Results of Observations

Table I shows the age and sex incidence of the five allergic diseases. Table II gives the percentage incidence of allergic diseases. Table III shows the duration of symptoms for each group. Drug allergy is of special interest

TABLE I.—*Age and Sex Incidence of Allergic Diseases*

Age	Asthma		Urticaria		Allergic Rhinitis		Atopic Eczema		Drug Allergy	
	M	F	M	F	M	F	M	F	M	F
0–1 ..	1		9	8			1			
2–4 ..	6		11	4	1		2			
5–9 ..	4	2	5	5		1	2			
10–14 ..	3	2	5	5	2					
15–19 ..	4		2	2		1				1
20–29 ..	3	2	1	2	2		1	2	1	
30–39 ..	6	9	4	1	6	4	6	1	2	2
40–49 ..	4	3	1	2	4	4	5	2		1
50–59 ..	4	9		3	1	3	1	1	1	2
60–69 ..		5		1	1			3		2
70+ ..	1			1						
Total ..	36	32	38	34	17	13	18	9	4	8
	68		72		30		27		12	

TABLE II.—*Incidence of Allergic Diseases*

	Asthma	Urticaria	Allergic Rhinitis	Atopic Eczema	Drug Allergy
Allergic cases ..	32·5%	34·5%	14·4%	12·9%	5·7%
Total practice of 4,000 patients	1·7%	1·8%	0·8%	0·7%	0·3%

TABLE III.—*Duration of Symptoms in Allergic Patients*

Duration	Asthma		Urticaria		Allergic Rhinitis		Atopic Eczema		Drug Allergy	
	M	F	M	F	M	F	M	F	M	F
<1 month ..		3	28	25			1		4	8
1– months ..	4		1	2			4	1		
3– „ ..	2		1	2	1		4	2		
6– „ ..	1	1					3	2		
1– year ..	2	4	3	3		2	2	2		
2– years ..	4	2	4	1	3	2	1	2		
3– „ ..	3	5				2	2			
5– „ ..	10	7	1	1	8	4	1			
10– „ ..	4	6			4	2				
15– „ ..	3	1			1	1				
20– „ ..	1	1								
30+ „ ..	2	2								

TABLE IV.—*Details of Patients Suffering from Drug Allergy*

No.	Sex	Age	Drug	Route of Administration	Manifestations
1	F	43	Phenylbutazone	Oral	Generalized urticaria
2	F	62	"Sulphatriad"	„	Skin rash, conjunctivitis
3	F	51	"Artane"	„	Generalized urticaria
4	M	35	A.T.S.	Intramuscular injection	Generalized urticaria, joint pains
5	F	67	Methylthiouracil	Oral	Agranulocytosis
6	M	28	Penicillin	Intramuscular injection	Generalized urticaria
7	F	57	"Acriflex"	Local application	Skin rash
8	F	18	Diphtheria immunization	Intramuscular injection	Generalized urticaria
9	F	35	Auristillae phenolis	Local application	Skin rash of face
10	M	56	Morphine hydrochloride	Subcutaneous injection	Circulatory collapse
11	F	38	Acetylsalicylic acid	Oral	Asthma
12	M	37	Streptomycin	Intramuscular injection	Generalized urticaria

TABLE V.—*Patients with Collateral Allergy*

No. of Patients	Sex	Main Complaint	Other Complaints
5	M	Asthma	Allergic rhinitis
12	F	„	„ „
1	F	„	Urticaria „
2	F	„	Atopic eczema
2	F	Urticaria	Allergic rhinitis
1	M	„	„ „
1	M	Atopic eczema	Urticaria „
1	M	Allergic rhinitis	Atopic eczema
1	F	„ „	„ „

from the therapeutic point of view, and details of the patients suffering from it are given in Table IV. Table V shows the patients with collateral allergy—that is, suffering from more than one form of allergic disease simultaneously. Such patients have been listed once only. They are included in the group which covers the most serious of their complaints—for example, a patient with severe recurrent attacks of asthma and also hay-fever is listed with the asthma cases. This is done to avoid duplicating the figures and to keep a true picture of the incidence.

Discussion

The figures given in the tables may not represent the actual incidence of the allergic conditions in this country, but they do give the true figures for this section of the population who come to the average surgery for these complaints.

Asthma.—Of 68 asthma cases, 45 fall within the working-age group (20 to 70 years), and 37 suffered from asthma for over five years. Although we are not discussing the management of asthmatics we would like to mention that our attitude towards these patients was similar to that which the average practitioner takes with his epileptic patients. They were encouraged to stay at work, kept under constant supervision, and invited to pay frequent visits to the surgery, not only for treatment, but to report their progress. The results were good, and most of them are usefully employed.

Urticaria.—Out of 72 patients 32 were under 5 years of age. As is well known, "spots" usually compel most parents to attend the surgery promptly, hence the high proportion of small children in this group. Table III shows that 53 cases were of the acute variety, lasting less than four weeks. Some mothers could trace the offending allergen to foods. Sheldon *et al.* (1953) explain the greater incidence of food allergy in children by the fact that small children appear to absorb undigested food particles more readily than adults.

Allergic Rhinitis.—As stated before, these figures may not represent a true picture of this condition. The general public tend to neglect or ignore the usual allergy, and the children who undoubtedly suffer from it are labelled as "tonsils and adenoids." Doctors often make this mistaken diagnosis. There were only 30 cases, and only one had the condition for less than six months. The rest had suffered for two years or more. One child under 5 was diagnosed, and only four patients aged 5 to 19. There were 23 cases over the age of 30. Table V shows that 20 allergic patients had allergic rhinitis as collateral allergy and were therefore not included in these figures.

Atopic Eczema.—This condition tends to occur with acute exacerbations, and the figures support this clinical finding. Only five children were affected by it, and 22 patients were over 20. Seventeen patients had this condition for less than one year, and only six had it for more than two years.

Drug Allergy.—In this group 12 patients suffered from definite drug allergy. In each case the symptoms lasted less than a month; 11 of the patients were over 20 years of age. The list of offending drugs becomes longer every day, and the incidence of drug allergy must vary with the habits of individual doctors in drug prescribing. The unjustified use of well-recognized potential drug allergens without clear indication will greatly alter these figures—for example, penicillin ointments and creams for all types of skin blemishes or sulphonamide tablets for elevation of temperature. We tend to avoid antibiotics in local applications, and do not use heavy metals and other drugs recognized to give a high incidence of drug allergy, especially if alternative measures will suffice. In fairness to the drug manufacturers it should be stated that certain drugs are often blamed as allergens when some inactive ingredient in the pill or medicine is the actual allergen. Indeed, some useful drugs have been banished into oblivion because of slight reactions which may have been wrongly attributed to their use. Lastly, drug allergy may give rise to some very serious and sudden reactions, and this should be kept in mind when drugs are given parenterally.

Summary

Observations were made for a period of twelve months on the incidence of five allergic conditions: asthma, urticaria, allergic rhinitis, atopic eczema, and drug allergy in a general practice.

Tables give the details of these observations.

The findings and their significance are discussed.

Special note is made of drug allergy.

REFERENCES

Freeman, J. (1950). *Hay-fever: A Key to the Allergic Disorders.* London.
Grant, D. K. (1953). *British Medical Journal*, **2**, 128.
Herxheimer, H. G. J. (1952). *The Management of Bronchial Asthma.* London.
Med. Offr, 1953, **90**, 3.
Pepys, J. (1953). *Postgrad. med. J.*, **29**, 351.
Pick, F. J., and Patterson, J. F. (1953). *British Medical Journal*, **2**, 605.
Rackemann F. M. (1953). *Practitioner*, **170**, 333.
Rubin, E. H. (1947). *Diseases of Chest.* Philadelphia.
Sheldon J. M., *et al.* (1953). *A Manual of Clinical Allergy.* Philadelphia
Siegal, S., *et al.* (1953). *J. Allergy*, **24**, 1.
Tuft, L. (1949). *Clinical Allergy.* London.
Vickers, H. R. (1952). *Practitioner*, **168**, 473.

EPIDEMIC OF INFECTIVE HEPATITIS IN AN OXFORD COLLEGE*

BY

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Infective hepatitis has long been recognized as a disease due to a specific micro-organism. This was Cockayne's opinion in 1912, and during the first world war and the next few years much work was carried out confirming this opinion, and distinguishing the disease from leptospiral infection and from other bacterial causes of jaundice (Willcox, 1919; Morgan and Brown, 1927; Gardner and Brown, 1928). In the years between the wars it became generally recognized that infection was usually spread by means of personal contact of some kind (Booth and Okell, 1928; Findlay *et al.*, 1931), and in 1939 Pickles emphasized the important part probably played by droplets from the respiratory tract.

During the second world war the aetiology of infective hepatitis again became an important problem owing to the high incidence of jaundice in the Forces. A number of epidemics in this country were studied with the greatest care (Newman, 1942; Ford, 1943; Lisney, 1944); and special efforts were made to correlate the observations made by Service medical officers, both British and American (Spooner, 1944; McFarlan, 1945; Gauld, 1946). Information collected in this way confirmed the importance of personal contact in the transmission of infection; but it was recognized that this contact was often of an indirect kind, and that the virus could be transferred as readily by fingers and feeding utensils contaminated with faeces or droplets as by direct droplet infection. Also during the war it was considered justifiable to carry out transmission experiments on human volunteers, and, by using material from patients in the early stages of the disease, it was found that infection could be transmitted by inoculation with serum and by oral and nasal administration of faecal suspensions (MacCallum and Bradley, 1944; Havens *et al.*, 1944; Neefe and Stokes, 1945).

As might be expected, from the discovery of the virus in faeces, food-, milk-, and water-borne outbreaks of infective hepatitis have occasionally been reported (Neefe and Stokes, 1945; Gauld, 1946; *Hlth Bull., Edinb.*, 1943; Read *et al.*, 1946). An epidemic of this kind occurred in an Oxford college towards the end of the Hilary Term, 1950, and, owing to a fortunate combination of circumstances, it was possible to be reasonably certain when infection took place and what article of food conveyed the virus to its victims.

History of the Epidemic

The Main Wave of Infection

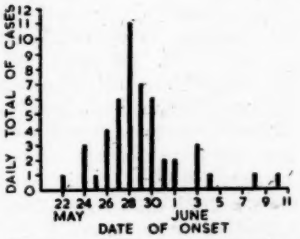
The outbreak first came to light on May 31, 1950, when three cases of infective hepatitis were diagnosed among undergraduate members of the college in question. Next day eight more cases were found, and on the day following another 12. These cases and all subsequent ones were distributed at random among those living in college, in college annexes, and in lodgings.

Once it was realized that an epidemic was in progress, inquiries were made, aimed at discovering any patients who had fallen ill before May 31 and who might be under the care of other practitioners. There were three such patients, including one who had begun his illness as far back as May 22, and this date has therefore been taken as marking the onset of the epidemic. From June 2, the day on which 12 cases were discovered, cases continued to appear with decreasing frequency for another week. The last patient in this wave of infection began his illness on June 10.

Incidence of Cases: May 22 to June 10

Date	Daily Total	Date	Daily Total	Date	Daily Total
May 22	1	May 29	7	June 5	0
„ 23	0	„ 30	6	„ 6	0
„ 24	3	„ 31	2	„ 7	0
„ 25	1	June 1	2	„ 8	1
„ 26	4	„ 2	0	„ 9	0
„ 27	6	„ 3	3	„ 10	1
„ 28	11	„ 4	1		

Between May 22 and this date—that is to say, during a period of 20 days—49 people had fallen ill with infective hepatitis, all connected in some way or other with the college, 47 of them being undergraduates. The table shows the number of cases occurring each day, and is accompanied by a histogram constructed from the figures.



Histogram of cases, showing distribution about a central peak.

Owing to its explosive nature the epidemic was regarded from the start as being due to a food- or milk-borne infection, and one of the first steps taken was to inquire among the kitchen and buttery staffs for any case of jaundice or "gastric 'flu" that had occurred four to five weeks previously. This inquiry proved fruitless, as did also all subsequent attempts to find an antecedent case that might have been the original source of infection.

Further light, however, was thrown on the problem on June 5 when a daughter of one of the college scouts and a patient of my practice attended surgery deeply jaundiced, having fallen ill seven days previously, on May 29—that is to say, at the height of the college infection. Next day I visited her in her home, and she admitted that she often had snacks of food in the college, and that about six weeks previously she had consumed a large plate of particularly delicious fruit salad and custard. She was quite sure that this was the only dish of food, apart from rolls and butter and pieces of cake, that she had eaten in the college during the previous few months. It seemed probable that she had acquired her infection from the same source as the undergraduate patients, and attention was therefore directed to the fruit salad and the custard as possible vehicles of the infective agent. On being questioned further, she remembered that she had eaten her helping of sweet on a Saturday evening, and that it had been left over from dinner on the previous day. Information was obtained from the college steward that fruit salad and custard had been served at dinner in hall on Friday, April 28.

At the suggestion of the medical officer of health, the problem of the date or dates of infection was next approached from a different angle. An attempt was made to discover a single meal or a small number of consecutive meals which had been eaten by all the undergraduate patients. It could be taken for granted that those living in college took their meals in hall regularly. So special attention was directed to the signing-in records of those patients who lived out of college, and who therefore lunched and dined in hall only occasionally. It was discovered that all patients in the living-out group either dined in hall on April 28 or lunched there on April 29. The menus showed that fruit salad and custard was served as a sweet on both occasions. These facts were consistent with the discoveries which had already been made about

*The Charles Oliver Hawthorne Clinical Prize essay for 1953.

the scout's daughter and her helping of sweet, and they contained the additional information that the custard was eaten on two consecutive days.

At this stage of the investigation the curious fact emerged that there were no cases of jaundice among the six members of High Table who dined in regularly, nor among the kitchen and buttery staffs, who were about 15 in number. No cases were in fact ever discovered among these groups, both of which included a proportion of young adults who, on the face of it, shared an equal risk with the undergraduates. Their escape was readily explained, however, when it was discovered that the dons had ice cream with their fruit salad, from a source outside the college; nor could there be much doubt that the kitchen and buttery staffs would have made the same choice also.

How the custard could have become contaminated was never discovered with any certainty. Presumably the virus might have gained access either to the milk from which the custard was made or to the custard itself at some stage while it was being prepared and handled. At any rate, contamination must have taken place inside the college, because had the milk been contaminated outside there would have been other outbreaks of infective hepatitis among those families and institutions which were supplied from the same source. From an inquiry carried out by the medical officer of health among general practitioners it was learnt that, although the incidence of infective hepatitis in the city was probably above the average, there was no widespread epidemic.

In order to account for the infection of those patients who missed dinner on April 28 and were presumably infected at lunch on April 29, it must be assumed that virus was carried over from one meal to the other. Custard was served at both, and it is probable that any left over from Friday's dinner would have been added to the fresh lot made for lunch on Saturday. Alternatively, receptacles which had been contaminated on the first day may still have contained sufficient virus, in spite of being washed up, to infect their contents on the second day. Although the washing-up arrangements in the college kitchen appeared to be very efficient, they may easily not have been thorough enough to destroy a relatively heat-stable virus.

A final piece of evidence in favour of the supposed dates of infection came to light later on, when it was discovered that an undergraduate guest from another college, who dined in hall on the suspected Friday night, fell ill with hepatitis on June 3—that is to say, near the peak of the college infection.

Secondary Cases

When infective hepatitis affects a closed community, a school for instance, it is common for a number of secondary cases to occur about a month after the primary wave of infection. The same thing often happens on a smaller scale in families. In the Oxford epidemic, however, probably owing to the fact that personal contact in a college is not very close, there were only three secondary cases, so far as could be discovered. One of these, the case of a patient who fell ill on June 30, came to light during the long vacation. The other two were reported during the following term after a notice asking for information on the subject had been displayed in the junior common-room. These latter were the cases of two friends who went on a hitch-hiking tour of France. One dated his illness from about June 20, and the other definitely from June 27, when he had an attack of "sunstroke," which was presumably the pre-icteric stage of infective hepatitis starting with acute febrile symptoms. Both these men were ambulant during most of the time they were jaundiced.

It could be argued that these three cases were a continuation of the main wave of the epidemic, and not due to secondary spread of infection. However, there was an interval of 10 days between the case already postulated as bringing the main wave of infection to a close and the first case of this second group. In addition, all these later patients fell ill between 23 and 33 days after the peak of the main wave on May 28. They all admitted to having had plenty of contact with earlier patients during the term, and could easily have acquired their infection in this way.

Clinical Description

The 47 undergraduate members of the college who were affected by the main wave of infection form a conveniently homogeneous group of patients, and it seems worth while to comment briefly on the clinical aspect of their illness. The majority of them were under my own care, although some only to start with, because I had as many of them as possible transported home by car as soon as they were fit to travel. Of the remaining few who were not under my care, through the courtesy of colleagues I was able to interview and examine all but one, an undergraduate who fell ill while at home and wrote later to say that he became jaundiced on June 2.

Besides the 47 definite cases of infective hepatitis there were two others, which may have been examples of subicteric infection. Both patients were undergraduates who developed symptoms suggestive of the pre-icteric stage of infective hepatitis, but who never became jaundiced or passed bile-stained urine, so far as could be observed. It must be remembered that minor gastro-intestinal disturbances of a non-specific kind are always common among the undergraduate population of Oxford during the summer months.

The onset of the disease was abrupt in all the patients except two, who began their illness with an insidious malaise and a gradual loss of appetite. The great majority fell ill suddenly with shivering, sweating, and generalized aches, starting on a definite day and at a definite time which they could remember. These symptoms were usually accompanied by headaches, and in two cases the clinical picture at this stage raised a suspicion of early poliomyelitis. In neither, however, was the headache accompanied by neck stiffness or any other signs of involvement of the central nervous system, and it was not thought necessary to perform lumbar puncture. Two patients started their illness with diarrhoea and two by fainting. In one, the general constitutional symptoms were accompanied by a widespread urticarial rash. A single patient had nose-bleeds, and two complained of local joint stiffness, but neither had signs of effusion. Only two patients had symptoms of irritation of the upper respiratory tract.

Patients rarely complained of specific symptoms indicative of disturbed hepatic function at the onset of their illness. Nausea or vomiting, sometimes accompanied by abdominal discomfort, usually became their most prominent symptoms when they had already been ill for a day or two, and when fever and generalized aches and pains were beginning to subside. Shortly afterwards, darkening of the urine was usually noticed, and at this stage many patients began to feel much less ill in themselves; although in all but the very mildest cases gastric symptoms persisted and gradually became more severe. In two cases nausea improved temporarily with the subsidence of fever, but became more severe again when bile appeared in the urine. One patient denied that his appetite was ever affected, although at the onset of his illness he had a temperature of 103° F. (39.4° C.). It was often difficult to tell when bile first appeared in the urine because accuracy in this respect usually depended upon the patient's own powers of observation, or upon the stage in his illness at which he first happened to be seen by the college sister or myself. So far as could be determined, the urine became bile-stained some time between the second and eleventh day of the illness. Among four patients under close observation from the onset of their symptoms, three developed obvious bile staining when they had been ill for six days and the fourth when he had been ill for three days.

The clinical records of the icteric stage in a large number of cases are incomplete because, as already mentioned, as many patients as possible were taken home by their parents, once the nature of their illness had been established. The cardinal symptom of jaundice was present in all cases, and appeared between the fourth and the fourteenth day of the illness, with a mean about the seventh day. No cases were found in which there was bile-staining of the urine without some degree of jaundice. In 16 cases the urine, as tested by the salicyl-sulphonic acid method, gave a positive reaction for protein. In 21 cases the liver was palpable and usually tender as well. This unexpectedly low figure is probably accounted for by the fact that many of the patients were seen only in the early stages of their illness. In seven cases the spleen was palpable, and in one of these it was also noticeably tender. There seemed to be no correlation between the presence of an enlarged spleen in the early days of the illness and the subsequent development of a severe or prolonged attack. In no case was a generalized enlargement of the lymphatic glands detected. Three patients complained of generalized pruritus. Total white-cell counts were carried out on two patients early in the icteric stage, and gave figures of 5,000 and 8,000 with a film of normal appearance in each case. No other special investigations were carried out.

As a rule, by the time that jaundice had appeared the patient was afebrile and feeling better, but occasionally fever and other constitutional symptoms persisted during the first few days of the icteric stage. This occurred usually in the more severe cases, which in addition showed persistent vomiting, marked prostration, and rapid loss of flesh. In a few cases the illness was so mild that the patient experienced only a transient digestive disturbance, and had completely recovered in less than a fortnight. However, as judged by the standard of cases seen in the Middle East during the recent war, most patients had an illness of moderate severity. An attempt was made to follow up the course of each patient's illness by sending out a request for information on the following points: (1) date of return of urine to normal colour; (2) date of return of normal appetite; and (3) date when the patient considered himself perfectly fit again and/or had regained any weight lost. Thirty-nine patients sent in replies during the long vacation.

An inquiry of this sort has obvious limitations, but the results of this one were clear-cut and consistent with previous experience of epidemic infective hepatitis. In approximately a third of the cases return of appetite and the reappearance of normal urine occurred after about two weeks' illness, and in another third after about three weeks. Among the remainder, a few took only a week to achieve normality, and the rest between four and six weeks. As was to be expected, convalescence was slow. About two-thirds of the patients took between three and five weeks to recover fully. Only three took a shorter time, and the rest between 14 and 16 weeks. Twenty-two patients reported loss of weight, two of them over a stone (10.9 kg.), and it was obvious that marked loss of weight was a feature of the disease in all but the mildest cases. The only notable symptoms reported as having occurred during convalescence were constipation and lassitude.

Two patients relapsed, one mildly and the other severely. The mild relapse was possibly precipitated by the consumption of alcohol. In the more severe case, relapse occurred four weeks after the onset of the initial attack, and while jaundice was still present. It began with an acute recrudescence of bilious symptoms. This patient took nine months to recover, but by the end of that time all tests of hepatic function were normal.

Discussion

Generally speaking, infective hepatitis is not a disease from which undergraduates suffer frequently. Apart from the victims of the epidemic described in this paper I have records of only six examples of the illness among rather more than a thousand undergraduate cases of all kinds seen during the four years 1946–50. Not only was the occurrence of the epidemic itself an unusual event, but the features of the epidemic and the circumstances under which it occurred also raised a number of points of interest.

Mode of Infection

Although there is no doubt that infective hepatitis is usually spread by personal contact, the pattern of the Oxford epidemic was strikingly similar to that produced by other infections known to have been spread by food or drink. In particular, it was explosive, and the distribution of cases was that which would be expected if infection had taken place during a short period of time, such as one or two days; their wide "scatter" being related to the long incubation period of the disease. The circumstances of the epidemic make it improbable that all the cases could have acquired their infection by simultaneous contact, either with a patient already suffering from the disease or with a symptomless carrier of the virus. A considerable number of the victims visited the college only for the purpose of eating their meals in hall, and these occasions could hardly have provided the opportunity for sufficient personal contact to account for such widespread distribution of infection within such a short space of time.

In infective hepatitis it seems probable that infection can be transmitted either by personal contact or by the consumption of some article of food or drink containing the virus. In the epidemic under discussion all the evidence pointed to a food- or milk-borne infection, and to custard served at two meals as the particular vehicle concerned. It was never discovered how contamination might have taken place, and it is only possible to surmise that, among those handling the custard, there was a symptomless carrier of the virus, or a subclinical case of infection. Certainly, had there not been a special lookout for suggestive symptoms, some of the milder cases in the college epidemic might well have escaped detection.

Incubation Period

If it is accepted that all cases occurring between May 22 and June 10 resulted from infection that took place on April 28 and 29, the range of incubation period in this epidemic was between 23 and 42 days. These are exact figures, because fortunately both the first and last patients to fall ill consumed only one of the two crucial meals—namely, lunch on April 29. This range is consistent with the findings in other epidemics. Pickles (1939) for instance, in a batch of 40 cases, in which case-to-case spread could be accurately traced, calculated incubation periods varying between 26 and 35 days. Gauld (1946) found a rather wider range of 15 to 41 days in his small epidemic of 11 cases affecting a mountain infantry regiment drawing its water supply for a limited period from a contaminated well; while Neefe and Stokes (1945) found that incubation periods in their holiday camp epidemic varied between 14 and 39 days. Figures of the same order were found by MacCallum *et al.* (1951) to hold good for the epidemic in East Anglia studied by the Jaundice Committee of the Medical Research Council during the period 1943–7.

Attack Rate

The dean of the college kindly supplied the information that 103 graduates dined in hall on April 28, and 138 lunched on April 29. There would have been considerable overlapping between these two groups, and the dean estimated that the total number of men who consumed one or both meals would have been about 150. Out of this 150, 48 fell ill with jaundice—47 members of the college and one guest. Taking into account also the scout's daughter, this gives an attack rate of about one in three. The same figure can be obtained from the description given by Read *et al.* (1946) of their epidemic of 24 cases occurring among medical students living in a hostel.

Summary

During the summer of 1950 an explosive outbreak of infective hepatitis took place in one of the smaller Oxford colleges. The total number of cases was 52—49 occurred within a period of 20 days and comprised the main wave of the epidemic; and 3, occurring later, constituted a minor secondary wave.

Evidence was obtained from which it was reasonable to deduce that this was a food-borne epidemic, the vehicle of infection having been custard that was served at a dinner and a lunch on consecutive specified dates. No certain source of contamination of the custard was ever discovered.

The attack rate among those exposed to infection at the two meals was about 1 in 3; and the incubation period ranged between 23 and 42 days. A histogram constructed from the number of cases occurring each day shows an approximately symmetrical distribution about a single peak, and corresponds to a mean incubation period of 30½ days with a standard deviation of 3½ days.

The epidemic showed no unusual clinical features. In most cases the pre-icteric stage consisted of a well-marked febrile episode. No cases of hepatitis, without obvious bile-staining of the skin or urine, were detected with certainty. The icteric stage varied greatly in severity and duration. Convalescence was frequently prolonged. There was a relapse rate of 4%.

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REFERENCES

Booth, W. G., and Okell, C. C. (1928). *Publ. Hlth, Lond.*, **41**, 237.
Cockayne, E. A. (1912). *Quart. J. Med.*, **6**, 1.
Findlay, G. M., *et al.* (1931). *Trans. roy. Soc. trop. Med. Hyg.*, **25**, 7.
Ford, J. C. (1943). *Lancet*, **1**, 675.
Gardner, A. D., and Brown, H. C. (1928). Report of Medical Research Council, 1927-8.
Gauld, R. L. (1946). *Amer. J. Hyg.*, **43**, 248.
Havens, W. P., *et al.* (1944). *Proc. Soc. exp. Biol., N.Y.*, **57**, 206.
Hlth Bull., Edinb., 1943, **2**, 64.
Lisney, A. A. (1944). *Proc. roy. Soc. Med.*, **37**, 165.
MacCallum, F. O., and Bradley, W. H. (1944). *Lancet*, **2**, 228.
—— McFarlan, A. M., Miles, J. A. R., Pollock, M. R., and Wilson, C. (1951). *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 273. London.
McFarlan, A. M. (1945). *Quart. J. Med.*, **14**, 125.
Morgan, M. T., and Brown, H. C. (1927). Ministry of Health Report on Public Health and Medical Subjects, No. 42. H.M.S.O., London.
Neefe, J. R., and Stokes, J. (1945). *J. Amer. med. Ass.*, **128**, 1063.
Newman, J. L. (1942). *British Medical Journal*, **1**, 61.
Pickles, W. N. (1939). *Epidemiology in Country Practice*. Wright, Bristol.
Read, M. R., *et al.* (1946). *Amer. J. Publ. Hlth*, **36**, 367.
Spooner, E. T. C. (1944). *Proc. roy. Soc. Med.*, **37**, 171.
Willcox, W. H. (1919). *Trans. med. Soc. Lond.*, **42**, 147.

"The precipitating cause of many malpractice actions is found in the unwise comments or criticism of physicians regarding treatment given to patients by other physicians. Commonly, it is criticism by a succeeding physician of the work of his predecessor on the case. Various authorities have estimated that 50 to 80% of all the suits for malpractice would be eliminated if such destructive criticism could be stopped. It is profitless to attempt to determine why physicians are so likely to criticize destructively and unethically, but the results of it are deplorable. Legitimate criticism can rest only on full knowledge of the facts as gathered from the physician who treated the patient, as well as from the patient."—Louis J. Regan, M.D., LL.B., *New Eng. J. Med.*, 1954, **250**, 463.

MONDOR'S DISEASE (SUBCUTANEOUS PHLEBITIS OF THE BREAST REGION)

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We should like to draw attention to an unusual condition characterized by the development of a subcutaneous cord in the breast region, usually along a line from the epigastrium to the axilla. The nature of this cord has given rise to speculation, but it appears to be of vascular origin, and we believe it to be a phlebitis and more particularly a periphlebitis.

The condition seems to be uncommon in this country, but, since it is self-limiting, medical advice may not be sought. Perhaps it is seen more in general practice than in hospital; some experienced general surgeons whom we have questioned have never met with it. It seems to be more common in France, where it is known as "maladie de Mondor," after Henri Mondor, who described cases in 1939, and who referred to it as "string phlebitis of the chest wall." Subsequent papers by Leger (1947), Kapitanoff, Touzard, Darbon, and Sicard (1950), and Kapitanoff and Küss (1950), all refer to it eponymously. But, in fact, the same condition was described in France in 1922 by Fiessinger and Mathieu, in America by Williams (1931) and Daniels (1932), and in this country by Robinson (1935). Adair (1950), in an article on cancer of the breast, stated that he had seen about 26 such cases over a period of 30 years, although most of them appear to have developed the lesion after a breast operation. He referred to it as a condition "which I have not found heretofore described" and which "has been confused with cancer." It is to Hughes (1952) that we owe the most comprehensive account of the disease in English. He gave details of five patients, on four of whom a biopsy was performed.

We describe five cases.

Case 1

An unmarried woman aged 50 attended hospital in July, 1951, having noticed, three weeks before, a tender cord below the breast. Her general health was good and she had had no recent illness, nor had there been a discharge from the nipple.

She was found to have a subcutaneous cord, approximately ¼ in. (6 mm.) in diameter, passing from the lower inner quadrant of the left breast to the left side of the epigastrium. Elevation of the breast made the cord stand out like a bowstring. In the breast, at the upper end of the cord there was indefinite induration, but this was not present when she was admitted a week later. The other breast and the regional lymphatic areas were normal. The breasts were well developed. We wondered whether this was an instance of lymphatic permeation from an occult carcinoma. A small portion of the cord and overlying skin were removed for examination.

Pathology.—In the subcutaneous fat there was a fibrous cord near the centre of which was a ring of smooth muscle. Within this ring was organizing tissue containing a few red cells. Outside the muscle there was connective tissue composed of collagen and fibroblasts with scattered elastic fibrils. In this tissue and around its edge were numerous capillaries. There was no suggestion of an elastic lamina. The cord was a blood vessel, probably a vein, containing thrombus, with marked fibrosis of the adventitia. Serial sections were cut and the cord was seen to divide. No malignant cells were seen. One near-by vessel also showed fibrosis of the adventitia.

When the patient was seen five months later no trace of the cord could be found.

Case 2

A married woman aged 54 was admitted to hospital in February, 1950. For two years the left nipple had been retracted. There had been pain under the breast for two weeks, but no discharge from the nipple.

The left nipple was indrawn and a little blood-stained fluid could be expressed. Passing down from the lower outer quadrant towards the costal margin was a cord attached to the skin and in the shape of an inverted Y. The breast tissue itself felt normal. The other breast was granular and there was a small mobile node in the left axilla. The cord was excised.

Pathology.—In two blocks taken from the specimen, one contained two small thick-walled blood vessels and the other a single larger vessel of the same type. The former were radicles of the larger vessel, which in serial sections was seen to divide. All lay in the subcutis and had narrow blood-containing lumina surrounded by a layer of plain muscle which was enveloped by a thick zone of cellular fibrous tissue containing scattered elastic fibres. No elastic lamina was present. Midway between the divisions of the affected vessel was a dilated lymphatic vessel, about which there were active inflammatory changes. In the subjacent breast tissue there was sclerosing adenosis.

The patient has been seen at frequent intervals, the last occasion being in January, 1953; no further lesion has developed.

Case 3

Mrs. E. K. Dawson, of Edinburgh University, very kindly sent sections from a similar case, and added that, so far as she could recall, it was the only example she had seen. We are indebted to her and to Mr. T. McW. Millar for details of the patient and for permission to record the case. We should add that we are responsible for the following interpretation of the sections.

FIG. 1.—Case 3. Showing a thin muscle band surrounded by a wide zone of fibrous tissue. The lumen is almost occluded by granulation tissue.

A married woman aged 53 was seen by Mr. Millar in June, 1951. In the right breast there was a centrally placed carcinoma, with *peau d'orange* over the lower half of the breast. A firm cord-like band, slightly tender, extended from the lower and outer angle of the breast and ran down the chest wall to the costal margin. On lifting the breast the band stood out, and it was obviously close to, and possibly adherent to, the skin. The lymph nodes in the right axilla and supraclavicular fossa were enlarged. A simple mastectomy was performed and a portion of the cord removed for examination. The patient subsequently received radiotherapy.

Pathology (Fig. 1).—The subcutaneous fat contained a single thick-walled blood vessel of similar type to those described in the other cases. Its lumen was reduced to a narrow crescentic slit by cellular and vascular granulation tissue which lay within a thin band of plain muscle. The main thickness of the vessel wall was, as in the other cases, due to a wide enveloping zone of compact cellular fibrous tissue in which there were irregularly scattered elastic fibres and a few capillary blood vessels.

Two months after operation the cord-like structure was very much less obvious.

Case 4

An unmarried woman aged 51 attended hospital in December, 1951. For two years she had had recurrent trouble from a small area in the left breast, which would come up like a boil and then subside without discharging. She felt unwell when the lesion was inflamed.

Examination showed a reddened indurated area about the size of a shilling in the skin and subcutaneous tissues over the lower inner quadrant of the left breast. A small bead of pus could be expressed. A thickening cord, thought to be a thrombosed vein, was felt running downwards and medially to the epigastrium. There were enlarged nodes in the axilla.

Subsequently the inflammatory area was excised. Histologically this was reported by Dr. R. H. Cowdell to be a subcutaneous giant-cell granuloma, probably of sebaceous origin. There was no biopsy of the cord in this case.

By the following month, the cord had subsided and there had been no recurrence when she was seen in July, 1953.

Case 5

One of us, through the kindness of Mr. Reginald C. B. Ledlie, was able to see this patient, a married woman of 57, who was found to have a tender subcutaneous cord which passed downwards and somewhat medially just lateral to the left breast. Five weeks later the cord was barely palpable, but she had developed a similar lesion in the right upper forearm. Some years ago she had had, in the left upper arm, a tender cord which resolved spontaneously.

Clinical Features

The essential lesion develops in the region of the breast, more commonly in the female. It is a subcutaneous cord which is often at first painful and tender, and which usually runs along a part or the whole of a line passing between the anterior axillary fold and the epigastrium. Usually, as in all these cases, it is below the nipple. Occasionally the cord divides into two or even three, and a case has been described in which a plexiform pattern existed. Earlier authors have described cases in which these cords were found elsewhere on the chest-wall, sometimes extending far down on to the abdomen. This is not surprising if the condition is to be regarded as a phlebitis, for the subcutaneous veins of the region (Fig. 2) have the same distribution as the cords.

Sometimes there is a history of recent local trauma or muscular strain, or of some pre-existing febrile episode or malaise, with or without an obvious local focus of infection, such as was present in Case 4. Case 3 was associated with a carcinoma of the breast, but there may be no symptoms or signs other than the presence of the cord.

The cord itself may be confused with cancer, as mentioned by Adair, and as happened in Case 1. It is possible for such a cord to be associated with an early carcinoma of the breast and for the patient for this reason mistakenly to be placed in an advanced stage and denied radical treatment.

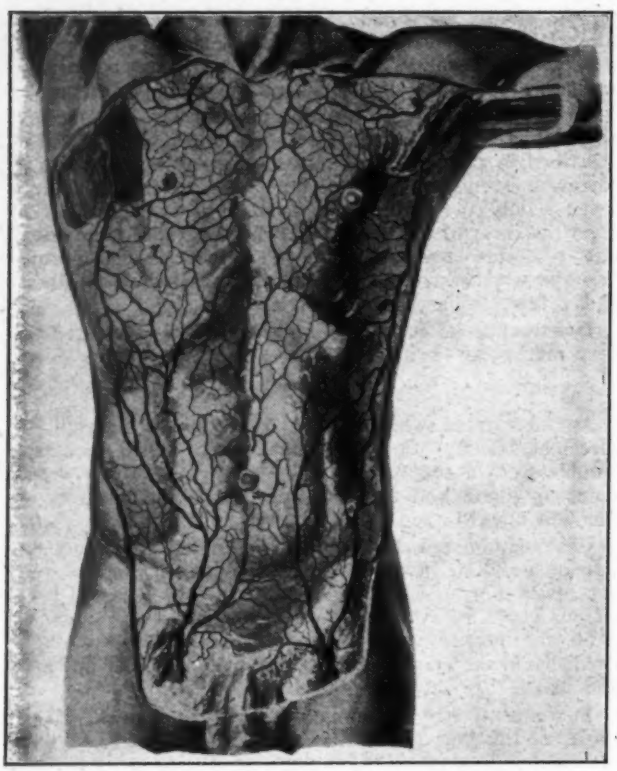

FIG. 2.—The subcutaneous veins of the anterior body wall. (Modified from C. W. Braune by Spalteholz, 1896.)

Pathology

The earlier authors (Fiessinger and Mathieu, 1922; Williams, 1931; Daniels, 1932; Robinson, 1935) attributed the lesion to a superficial thrombophlebitis, although in none of their cases was a histological examination made. Mondor (1939) described the histology in one case and concluded that the cord was either a lymphatic vessel or a vein, and favoured the former as no red blood cells were seen. Sicard (Kapitanoff, Touzard, Darbon, and Sicard, 1950) found a thrombosed vein without periphlebitis. Hughes (1952), however, prefers the term "angiitis," and considers the essential lesion to be gross sclerosis around the vessel.

In the present series the three specimens examined all contained red blood cells, so that a lymphatic origin can be discounted, although it is of interest to note that in Case 2 a neighbouring lymphatic vessel was affected by the inflammatory change.

The distinction between an arteritis and a phlebitis is difficult to make, and Hughes prefers the wider term of "angiitis." However, we consider that from the thinness of the muscle band and the paucity of elastic fibres it is much more likely to be of venous origin; furthermore, analogy with similar lesions elsewhere and the location of the cords (Fig. 2) support the view that it is a phlebitis. A striking feature of the lesion is the wide zone of fibrosis around the vessel, a point stressed by Hughes.

Moschcowitz (1933) gave details of six patients who presented a similar picture of a subcutaneous cord in the breast region. He examined the cord in one case and found an epithelial structure surrounded by leucocytes. He attributed the lesion to inflammation of a persistent mammary line and termed the condition "vestigial mastitis." We agree with Hughes that photomicrographs of the condition are difficult to interpret. In none of the other reported cases has such an epithelial structure been found.

No wholly satisfactory name has been found for the condition; among those suggested have been "string phlebitis" and "phlébite en cordon," both of which are concise and describe the clinical features: Hughes favours "sclerosing peri-angiitis of the lateral thoracic wall," a term which describes the pathological features, but which is clumsy and leaves doubt about the type of vessel affected. Although Mondor was not the first to describe the condition, he was the first to study it in detail, and, as we have an affection for the eponymous, we have used the short term "Mondor's disease."

Aetiology

In three of our cases there was no apparent cause. In Case 4 it is difficult not to incriminate the infected sebaceous cyst, which was situated at one end of the cord. In Case 3 the connexion between the thrombosed vein and the breast carcinoma is not clear. Robinson (1935) attributed the lesion to muscular strain: one of his patients had been digging in the garden and the other moving heavy furniture. He compared it with the axillary "phlébite par effort." (It should, however, be mentioned that it is often the exercising of the arm that stretches the thrombosed vein and draws attention to its presence.) The French authors have also noticed the traumatic factor, and a pre-existing influenza-like illness in some cases. Adair (1950), noting the condition in post-operative cases, believes that in the majority it is "unquestionably due to too tight an application of the adhesive over the dressings, blocking the return circulation of the superficial breast veins to the axillary and subclavian veins." It is similarly possible for the breast support worn to impede the venous flow, especially when the breasts are well developed. The reason for the marked periphlebitis is not easy to determine. It is difficult not to postulate an infective agent, as was in fact present in the region in Case 4, and as was suggested by the spread of the inflammation to a lymphatic in Case 2. Clearly, many factors may be concerned in the production of phlebitis here as elsewhere in the body, and none of these factors may be obvious in a given case.

Progress and Treatment.—The lesion itself is self-limiting, and the "idiopathic" variety will resolve without treatment in a few weeks. There is no record of any case proceeding to suppuration. Any associated condition will naturally require the appropriate treatment.

Summary

Attention is drawn to the apparently little-known condition of Mondor's disease (subcutaneous phlebitis of the breast region), five cases of which are recorded.

The clinical features are described and the pathology and aetiology of the malady discussed.

The disease is in itself benign and self-limiting, and may be commoner than is supposed.

We are grateful to Sir James Paterson Ross for his help and encouragement, and for permission to publish Case 1; to Mr. C. E. Shattock for Case 2; to Mr. A. Elliot Smith for Case 4; and to Mrs. Dawson for her help. We should also like to thank Dr. J. W. Whittick and Dr. R. J. R. Cureton for considerable help with the histology.

REFERENCES

Adair, F. E. (1950). *Practitioner*, **165**, 473.
Daniels, W. B. (1932). *Amer. J. med. Sci.*, **183**, 398.
Fiessinger, N., and Mathieu, P. (1922). *Bull. Soc. Méd. Hôp. Paris*, **46**, 352.
Hughes, E. S. R. (1952). *Aust. N.Z. J. Surg.*, **22**, 17.
Kapitanoff, G., and Küss, M. G. (1950). *Mém. Acad. Chir., Paris*, **76**, 945.
—— Touzard, Darbon, and Sicard, A. (1950). Ibid., **76**, 939.
Leger, L. (1939). *Presse méd.*, **55**, 849.
Mondor, H. (1939). *Mém. Acad. Chir., Paris*, **65**, 1271.
Moschcowitz, A. V. (1933). *Ann. Surg.*, **98**, 855.
Robinson, R. H. O. B. (1935). *Brit. J. Surg.*, **23**, 296.
Spalteholz, W. (1896). *Handatlas der Anatomies des Menschen*. Hirzel, Leipzig.
Williams, G. A. (1931). *J. Amer. med. Ass.*, **96**, 2196.

PULMONARY OEDEMA DUE TO LATENT PHAEOCHROMOCYTOMA

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The somewhat rare condition of phaeochromocytoma is occasionally diagnosed, but is all too often a necropsy diagnosis. Death is usually due to cerebral haemorrhage, pulmonary oedema, or ventricular fibrillation (Wood, 1950). In the case reported below an unsuspected phaeochromocytoma caused pulmonary oedema during a planned operation for repair of inguinal hernia.

Case History

A robust man of 60 complained of left sciatic pain, thought to be due to a truss he was wearing for a left inguinal hernia. He was admitted to hospital for repair of this hernia. He was robust and apparently in good health : his pulse rate in bed was 60 a minute and blood pressure 140/80 mm. Hg. For the operation he was given premedication morphine, 1/6 gr. (11 mg.), and atropine, 1/100 gr. (0.65 mg.), one hour before operation. Anaesthesia was induced with thiopentone, 0.4 g., and gallamine triethiodide, 80 mg., and maintained with cyclopropane, ether, and oxygen in a closed circuit. A No. 4 Waters airway was inserted. He was placed supine on a horizontal operating table. Respiration was almost adequate by the time he was on the table, and was assisted.

Some 20 minutes after the operation had begun the pulse became irregular at a rate of 80 and cyclopropane was discontinued. The pulse irregularity ceased almost at once, but the rate increased gradually to 120 ; in the course of a few minutes his skin colour changed from pink to blue and then to grey, the respiration rate increased and moist sounds were noticed, first in the trachea and then in the lungs. The face-mask was removed and mucus aspirated from nose and pharynx. When this had been done he was almost conscious and would not tolerate the airway. The operation had been completed, so he was returned to the ward. There he was conscious and reacted to questions, but cyanosis gradually increased, breathing became laboured, and he was distressed : his pulse rate was about 140 and irregular. It was realized that he had developed heart failure with pulmonary oedema of unknown cause. Oxygen was given by B.L.B. mask and from an Oxford inflator. Nikethamide was given intravenously, two doses of 2 ml. ; aminophylline, 0.5 g. intravenously ; morphine, ¼ gr. (16 mg.) intravenously, with no improvement. Death occurred approximately three and a quarter hours after induction of anaesthesia.

At necropsy the lungs were congested and waterlogged, and blood-stained froth was present in all the passages. A haemorrhagic tumour, 2 in. (5 cm.) in diameter, was found in the left adrenal gland ; this proved to be a phaeochromocytoma. The histological appearance was typical, the tumour consisting of sheets and columns of polygonal cells separated by a rich plexus of sinusoids with which the cells were in intimate contact. A weak chromaffin reaction was given by these cells when fixed in a solution containing potassium dichromate.

Comment

Macintosh and Mushin (1946) describe how pulmonary oedema may develop during anaesthesia in the presence of an obstructed airway. In this case there was no respiratory obstruction. Death was due to congestive heart failure and pulmonary oedema, which probably followed a sudden rise in blood pressure and perhaps ventricular fibrillation due to outpouring of adrenaline or *nor*adrenaline. It is uncertain why this developed during operation, but release of histamine at the site of operation may be concerned. Small injections of histamine lead to a fall in blood pressure, and following this there may be a rise in blood pressure above the normal, due to a compensatory secretion of adrenaline (Samson Wright, 1952). The mechanism in this compensation is probably the fall in blood pressure via the carotid sinus, thence via the nerve to the adrenal gland. During operation in normal subjects this complex would be unnoticed, there being no change in blood pressure, but in the presence of phaeochromocytoma it is possible that the secondary overaction of the adrenal glands may be exaggerated.

According to Graham (1951) a potentially fatal paroxysm may be induced by the anaesthesia or by the positioning of the patient. Ward, Riches, and Johnson (1952) discuss anaesthesia for removal of phaeochromocytoma. They advise against drugs which affect the myocardial irritability or cardiac rate, such as cyclopropane, trichlorethylene, and gallamine, and point out that high concentrations of ether may limit any rise in blood pressure. They recommend the use of benzodioxane to limit rise of blood pressure, and intravenous injection of procaine amide to control gross cardiac irregularity. Cobb *et al.* (1953) report the successful control of blood pressure by benzodioxane and L-*nor*-adrenaline during surgical removal of a phaeochromocytoma.

The tragedy in this case is that the patient's wife revealed after his death that for two years he had had attacks of palpitations, faintness, sweating, and pallor lasting a few minutes, followed by a sensation of exhaustion. These are very like the paroxysmal attacks described by Smithwick *et al.* (1950). The patient was ashamed of these attacks and did not mention them before operation.

Summary

A case is described in which death occurred due to pulmonary oedema which developed during a planned operation for inguinal hernia. Necropsy revealed a phaeochromocytoma of the left adrenal gland which caused the pulmonary oedema.

We would like to express our thanks to Mr. K. H. Taylor, under whose care the patient was admitted, for permission to publish the case; to Dr. L. E. Glynn for the necropsy report; and to Dr. H. J. Harris for assistance in the preparation of this article.

REFERENCES

Cobb, C. C., Hall, J., and Hall, R. A. (1953). *Lancet*, **1**, 973.
Graham, J. B. (1951). *Int. Abstr. Surg.*, **92**, 105.
Macintosh, R. R., and Mushin, W. W. (1946). *Physics for the Anaesthetist*, p. 203. Oxford.
Smithwick, R. H., Greer, W. E. R., Robertson, C. W., and Wilkins, R. W (1950). *New Engl. J. Med.*, **242**, 252.
Ward, G. E. S., Riches, E. W., and Johnson, B. (1952). *Arch. Middlx Hosp.*, **2**, 133.
Wood, P. (1950). *Diseases of the Heart and Circulation*, p. 421. London.
Wright, Samson (1952). *Applied Physiology*, 9th ed., pp. 337, 554. London.

The hygiene of seafarers has been receiving attention from a joint International Labour Organization and World Health Organization committee in Geneva. The chairman was the vice-president of the International Shipping Federation, Norway, and Dr. W. M. Frazer, emeritus professor of public health at Liverpool, was vice-chairman. The main recommendations concern the provision of medical advice by radio, the equipment of medicine chests, and the examination of all new entrants to the Merchant Navy for tuberculosis. In general the radio facilities are considered now to be satisfactory. The committee drew up a list of minimum requirements based on the *International Pharmacopoeia* for the medicine chests of ships not carrying a doctor. The drugs in the chest are intended for use by the master on his own initiative in the case of minor ailments and after wireless advice in serious illness.

Medical Memorandum

Uterine Abnormalities in Sisters with Associated Android Features

Since the introduction of hysterosalpingography, and its increasing use in the investigation of infertility, the discovery of congenital uterine abnormalities has become increasingly common. However, uterine malformation in sisters is extremely rare, and with android features is of special interest.

Case Report

A married woman aged 29 first attended the gynaecological out-patient department with a history of amenorrhoea and morning sickness for four months. The menarche occurred at 18. The menstrual cycle was 10–12/50–60 days. She had been married five years. There was involuntary infertility.

On examination a thick-set muscular female with marked hirsutism of face, trunk, and limbs, and male distribution of pubic hair, was seen. Her height was 5 ft. 2 in. (157.5 cm.). Blood pressure was 140/90. Her breasts were well developed, with prominent Montgomery tubercles. Vaginal examination revealed the uterus enlarged, consistent with a ten-weeks pregnancy, and there was moderate hypertrophy of the clitoris. She was referred to the antenatal clinic, where arrangements were made for her confinement in hospital.

At subsequent visits the uterus was noted to be asymmetrical, with a diffuse swelling to the right which could not be felt apart from the body of the uterus. At the 35th week of pregnancy she was admitted to hospital with the signs of mild pre-eclamptic toxaemia and an unstable presentation. As there was no cephalo-pelvic disproportion a uterine malformation was suspected. The toxaemia worsened in spite of rest and sedation, and, because of this and the unstable presentation, delivery by caesarean section was decided upon. At operation a bicornuate uterus was found with the pregnancy contained in the left horn. The adrenal glands were not palpated, but both ovaries appeared to be normal. A male child weighing 6 lb. 2 oz. (2.8 kg.) was delivered, and the patient made an uninterrupted convalescence, being discharged from hospital on the 17th day of the puerperium with the child breast-fed.

Further investigation was undertaken three months after delivery. By this time the child was no longer breast-fed and menstruation had been re-established. A hysterosalpingogram confirmed the presence of a bicornuate uterus, and intravenous pyelography showed a normal urinary tract. Urinary 17-ketosteroids amounted to 14.5 mg. in 24 hours. *X*-ray examination of the skull showed a normal pituitary fossa.

Family History

On being informed that she had a double womb, the patient volunteered the information that her elder sister had been investigated at another hospital for a similar abnormality. Information from this hospital stated that this sister had been admitted with a threatened miscarriage, which had completed itself shortly after admission. Examination under anaesthesia had revealed a septate bicornuate uterus, a sound having been passed 9 cm. into the left horn and 11 cm. into the right, but hysterosalpingography had not been performed.

The elder sister agreed to attend the gynaecological out-patient department. She was 31 ; the menarche had occurred at 17, and the menstrual cycle was 6–8/35–40 days. She had been married nine years, and had had two pregnancies, both having terminated spontaneously at the 10th week. Examination revealed hirsutism, but to a less degree than in the above case, and hypertrophy of the clitoris. Urinary ketosteroids were 8 mg. in 24 hours. A hysterosalpingogram showed a bicornuate uterus with non-patency of the right Fallopian tube.

The third and youngest sister, aged 22, also agreed to examination. The menarche had occurred at 14, and the menstrual cycle was 5–7/28 days. She was unmarried and nulliparous. Examination showed normal female hair distribution with normal external genitalia. Vaginal examination and hysterosalpingography, performed under general anaesthesia, revealed a normal uterus.

The three sisters had been born and brought up in Ireland and had no brothers. The mother, who still lived in Ireland, apparently had hirsutism, but unfortunately no record could be obtained of the uterus ; it had been removed some 15 years previously for menorrhagia.

Comment

It does not seem unreasonable, in these cases, to assume a relationship between the uterine abnormalities and the presence of minor degrees of female pseudohermaphroditism, represented by the hirsutism and hypertrophy of the clitoris —the two conditions being produced by the action of androgenic hormones of adrenal cortical origin, in early foetal life, inhibiting normal fusion of the Müllerian ducts, and producing the android features. Greene (1944) produced female hermaphroditism experimentally in animals by subjecting the female foetus to the influence of androgenic hormones, and in these cases various uterine abnormalities also were produced. An example of this occurring in animal life is the sterile freemartin ; here the androgenic hormone reaches the female foetus via the placental circulation. However, in experimental cases of intersexuality the earlier the influence of the androgenic hormones in foetal life the greater the degree of sex reversal. Also, as normal fusion of the Müllerian ducts has occurred by the 14th week of intrauterine life, one would expect a much greater degree of sex reversal than in the present case. In Young's (1937) series of female pseudohermaphrodites the uterus appeared either to be normal or to be absent.

Heredity.—That this factor plays a part in the production of female pseudohermaphrodites is well known, especially in its lesser degrees (Browne, 1950). Biggs and Rose (1947) were able to collect nine families affected in this way : two sisters were pseudohermaphrodites, and in four of these families both males and females were affected. That uterine malformations arising from failure of fusion of the Müllerian ducts may also be hereditary has been shown by Way (1945, 1947). In his series there were four cases in which the mother and female child both had uterine abnormalities of this type, and in one of these cases two sisters were so affected. Hunter (1950) recorded 32 cases of uterine abnormalities and added one in which the mother had a fundal depression and the daughter a uterus bicornis bicorpus unicollis.

Unfortunately, in our three cases it was not possible to obtain information about the mother's uterus, but the fact that she was hirsute is suggestive that she may have been similarly affected.

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References

Biggs, Rosemary, and Rose, Elizabeth (1947). *J. Obstet. Gynaec. Brit. Emp.*, **54**, 369.
Browne, F. J. (1950). *Postgraduate Obstetrics and Gynaecology*, p. 398. London.
Greene, R. R. (1944). *J. clin. Endocr.*, **4**, 335.
Hunter, W. (1950). *J. Obstet. Gynaec. Brit. Emp.*, **57**, 721.
Way, S. (1945). Ibid., **52**, 325.
—— (1947). Ibid., **54**, 469.
Young, H. H. (1937). *Genital Abnormalities, Hermaphrodites, and Related Adrenal Diseases*. Baltimore.

Reviews

WAR SURGERY

Surgery of Trauma. Edited by Colonel Warner F. Bowers, M.C., U.S.A. With Forewords by Melvin A. Casberg, M.D., and Surgeons General of the Army, the Navy, and the Air Force. (Pp. 605; 284 illustrations. £6.) Philadelphia and London: J. B. Lippincott Company. 1953.

This book represents a considered review of war surgery based on the experiences of the medical officers of the armed forces of the United States in the second world war and the Korean war. It contains chapters written by 42 contributors, all but four of whom are officers or ex-officers of one of the fighting services.

As is inevitable in a composite work of this kind, the chapters vary considerably in their scope and their quality. The variation in scope is well seen in two adjacent chapters. Chapter 15 on vascular wounds occupies 34 pages, and, apart from a diatribe against tobacco, is chiefly concerned with peacetime technique. Chapter 16, on fractures occurring in war wounds, deals with the whole of this important subject in 17 pages, of which three and a half are devoted to reproductions of radiograms, yet succeeds in giving a lucid and admirable summary of the principles of treatment, illustrated by case reports.

There are four sections devoted respectively to the physiological aspects of the management of trauma, to regional wound surgery, to military considerations in wound management, and a short final one on research methods. Of these the second is by far the most successful. The writers on general principles know a good deal more about their subjects than about the art of clear writing, and they tend to dump down a mass of unsorted statements and unproved theories for the reader to sort out in his own time and in his own way.

Most of the chapters in the regional section are excellent; the best is Chapter 6, on cranio-cerebral trauma, by Donald Matson. He knows his stuff and knows how to write simply and clearly and to make every figure earn the space it occupies. Chapter 18 on amputations, by Leonard T. Peterson, makes a welcome retreat from the advocacy of guillotine amputations that was the official policy of the American army during the second world war. Dr. Peterson says, "The open amputation was known previously as the guillotine amputation." It was not. A war amputation, with or without flaps, should always be open, and no surgeon with any knowledge of warfare has ever advocated primary suture of an amputation stump. A guillotine amputation was one with no flaps. The fault of the guillotine amputation, and of many of those illustrated in this chapter, is that it involves needless sacrifice of tissue and usually two operations, and offers no additional safety. One of the most detailed, as well as one of the best, chapters is that on genito-urinary wounds, by Colonel James Kimbrough, who during Hitler's war made many friends in Britain. The pages on the management of the neurogenic bladder are admirable.

The book is well produced and contains an immense number of facts and figures. It is a work of reference rather than a guide for the young surgeon, but to the expert, knowing what he wants and where to look for it, it will prove a mine of factual information.

HENEAGE OGILVIE.

PREVENTIVE MEDICINE

Textbook of Preventive Medicine. By Professor Hugh R. Leavell, M.D., Dr.P.H., and Professor E. Gurney Clark, M.D., Dr.P.H. With the assistance of 19 collaborators. (Pp. 629; 28 figures. 68s.) London: McGraw-Hill Book Publishing Co. 1953.

This book is not a textbook according to the generally accepted meaning of the term in this country. Indeed, the authors specifically state that it should be used as a compendium, that it is not a textbook of epidemiology or of biostatistics, and that it is not intended as a course in public health administration. The chief aim is to advance a philosophical concept and methods of approach to preventive medicine. It is designed mainly for the doctor entering private practice. Dr. Leavell is professor of public health practice at Harvard School of Public Health and Dr. Gurney Clark is professor of epidemiology at Columbia University. Those collaborating are drawn from many American universities and state and city health departments.

The authors wisely decline to attempt to distinguish between "public health" and "preventive medicine." They prefer to consider how the public health officer practises preventive medicine and how the family practitioner applies it—a neat, sound, and subtle distinction. The main sections of preventive medicine are all considered with great care—epidemiology, infectious diseases, nutrition, chronic illness, cancer, maternity and child welfare, mental health, and occupational health. There is an excellent chapter on biostatistics—a subject not too easily assimilated by most doctors, but this makes applied mathematics easier. The few pages on tests of significance provide a most useful and salutary restraint on enthusiasm in assessing ascertained facts.

There is much in this book about American agencies and services, and it is therefore naturally of more use to the American than to the European doctor, but even so a general knowledge of administrative arrangements in the States is useful to us for reference. But most of the chapters are of direct interest and will supply valuable stimulation in all countries where English is read or translated. The extensive references and indications for additional reading give guidance to the reader who may wish to pursue any of the extraordinary variety of special subjects referred to. The paper and binding are superlative. The printing is so unusually good that the middle-aged presbyope may enjoy the unusual experience of reading comfortably without spectacles subject to suitable remoteness of the volume. The British reader who can afford the price will be the fortunate possessor of a book which will be less useful for reference than the standard British textbooks on public health and than at least one American textbook. But it will certainly set him off on new lines of approach to preventive medicine.

C. METCALFE BROWN.

TEXTBOOK OF GYNAECOLOGY

Textbook of Gynecology. By John I. Brewer, B.S., M.D., Ph.D. (Pp. 532; 146 illustrations. 76s. 6d.) London: Baillière, Tindall and Cox. 1953.

Dr. Brewer's previous book was entitled *Gynecology* and presented the subject entirely from the standpoint of symptoms, thus reflecting the teaching plan of the gynaecological department in the medical school of the Northwestern University of Chicago. It now forms the basis of Part 2 of this new work, the first part having been added to supply the undergraduate with a more systematic account of disease to which he can refer when he leaves the bedside. Both sections are neat and compact, but the reasonable size of the book is mainly explained by the omission of embryology, anatomy, physiology, and operative treatment, and by the proper restriction of the place given to endocrine therapy. While expressing views on the pathology of certain diseases which differ from those held by most gynaecologists in Britain, the author impresses the reader by his simple common-sense advice on the handling and treatment of the patient and her complaint. The illustrations are nearly all photographs and do full justice to the art of modern photography.

The main criticism which might be levelled against the book is that the allocation of space fails to indicate or misrepresents the relative importance and frequency of various diseases. Thus Paget's disease and hydradenoma of the vulva receive as much, if not more, attention than does Bartholin cyst; and cervical pregnancy and amoebic vaginitis appear to be as important as adenomyoma of the uterus.

The dual approach to the same subject inevitably means some repetition, but this has its advantages. It is unfortunate, however, that the layout makes its necessary to consult four different chapters in order to get a composite picture of the treatment of fibroids and their complications. The selection and arrangement of subjects for an undergraduate textbook of gynaecology is extraordinarily difficult, and most of the problems can be solved only at the expense of creating others. No author can hope to do more than achieve a credit balance, and Dr. Brewer has certainly succeeded in doing this.

T. N. A. JEFFCOATE.

DIABETES AND ASTHMA

Zur Genese des Diabetes Mellitus und des Bronchialasthmas. By Professor M. Bauer. (Pp. 113. M. 9.60.) Stuttgart: Georg Thieme. 1953.

This is a difficult book to appraise and is concerned with the genesis and nature of diabetes and asthma. It appears to be the forty-ninth book produced in a series on "Work and Health," under the aegis of the German "Ministry of Work." One rather feels that this Ministry must have said to the appropriate authors, "Keep writing and we will publish."

The major part of this book is concerned with diabetes. First, the relation of trauma to the production of diabetes is discussed and no clear connexion found. The relation of the total endocrine system is then considered, and the well-known cycles of carbohydrate metabolism adequately described. Clear, but nothing new. Asthma is treated under two similar headings: is it of pure allergic origin, or does trauma (*schadigungsfolge*), including infections, and particularly bronchial ones, give the answer? The answer is elusive.

Only two sections have a reference section, fairly international. But when the writer of the introduction quotes seven German writers by name "*as well as* Banting and Best and others" as concerned in the discovery of the relation of the pancreas to diabetes, it leaves a blatantly Germanic and sour taste in my mouth.

R. D. LAWRENCE.

FORENSIC MEDICINE

Forensic Medicine: A Textbook for Students and a Guide for the Practitioner. By Douglas J. A. Kerr, M.D., D.P.H., F.R.C.P.(Ed.), F.R.S.(Ed.). Fifth edition. (Pp. 362; illustrated. 28s.) London: Adam and Charles Black. 1954.

This popular Scottish students' textbook appears in a fifth edition after an eight-year interval. It will be most welcome to a wide circle of both students and general practitioners who desire a concise practical guide to the subject, yet never intend to practise the art themselves. The author writes this time with the newly vested authority of the regius professorship at Edinburgh. Kerr's book has always been sound, lucid, and remarkably well illustrated: we find no change in the easy digestibility of any subject he sets out so succinctly, whether on the dry bones of legal procedure in case of death or on the more arresting subjects of wounds, asphyxia, or the sex offences: Kerr has obviously seen them—and taught on them.

This book, already distinctly fatter than its predecessors, must not grow larger. It is not a comprehensive guide to the subject, and to become voluminous would be to court disaster. It covers a remarkably large field, and Kerr has incorporated new legislature (Cremation Act, 1952, Coroners' Rules, 1953, and newer Poisons Regulations) in order to keep abreast of the times. An interesting short chapter on the history of the subject appears in this edition. A few minutiae are still dated—like the reference to "veronal" as "the most common soporific to cause poisoning," and "deaths from chloroform occur under surgical anaesthesia." We note, too, an anachronism on the wording of the English coroners' suicide verdict—which no longer uses the words "temporarily insane"—and uncertainty on the spelling of M'Naghten and even Romberg. The references for further reading must have attention next time, for they do not appear to have taken adequate notice of the many contributions to the literature in the subject that the last 10 years have brought. But, by and large, Kerr has done a good job on the text, largely by leaving it well alone, modernizing only its law and statistics. It can be strongly recommended to the student and the general practitioner who wants everyday guidance.

KEITH SIMPSON.

HERNIA

Anatomy and Surgery of Hernia. By Leo M. Zimmerman, M.D., and Barry J. Anson, Ph.D.(Med.Sc.). (Pp. 374; 204 figures. 76s. 6d.) London: Baillière, Tindall and Cox. 1953.

This volume is the result of collaboration between a surgeon and an anatomist, both of the highest standing and wide experience. It is finely produced and superbly illustrated, and it may be taken as the last word in American experience. Naturally it deals for the most part with familiar material and with established methods, but these are well presented and illustrated with quite remarkable accuracy. Every class of hernia is described in elaborate detail, but we do not think that sufficient stress is laid on the importance of the neck of the sac. It is our own belief (we may be wrong) that when strangulation occurs it is invariably at the neck of the sac and physically due to abnormal thickening at this point. In the case of femoral hernia this is of vital importance, for if it is true the femoral ring itself is of quite secondary import. However this may be, the anatomical drawings here presented are of a very high order and worthy of close study.

The chapter by Bettman on diaphragmatic hernia deserves special mention. It gives a full and clear account of this difficult and important condition, and again the illustrative drawings are a pleasure to study and are of real value.

HENRY SOUTTAR.

NEUROLOGY AND PSYCHIATRY

Progress in Neurology and Psychiatry: An Annual Review. Volume VII. Edited by Professor E. A. Spiegel, M.D. (Pp. 604. 75s.) London: George Allen and Unwin. 1953.

The association of neurology and psychiatry is closer in the United States than in Great Britain, where co-operation between the two disciplines is exceptional. Professor Spiegel, however, believes that "there is hardly a field of medicine in which the interrelationship between clinic and laboratory work is as obvious as in neurology and psychiatry."

This comprehensive book is the work of 73 contributors; the only non-American authors are Professor Sjögren and Dr. Hallgren (Stockholm), who write on genetics. The book is in four parts: the basic sciences (neuro-anatomy and neuro-physiology), neurology, neurosurgery, and psychiatry. Each contributor, an authority in his own sphere, surveys the abundant literature with a critical eye. The weekly, monthly, and quarterly spate of papers is so great that the postgraduate student finds it difficult to separate the wheat from the chaff. The chaff of this book is negligible, and although the wheat has a particular flavour it is nevertheless genuine wheat.

The psychological aspects of psychiatry receive less prominence in the volume than the physiological. While there are chapters on the neuroses, psycho-analysis, group psychotherapy, and rehabilitation, the book nevertheless gives the impression that the psyche as such is not of vital interest to the editor. The contribution on clinical psychiatry is particularly good, and there are notable chapters in Part I on general and regional physiology.

No one will read this book from cover to cover, for it is essentially a book of reference for the hospital or medical library. Few librarians—provided funds permit—would care to be without it. The general arrangement is clear and the index is good, although it omits the names of the writers mentioned in the host of references given with each chapter.

E. A. BENNET.

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SOCIAL INCIDENCE OF RHEUMATIC FEVER

For many years it has been recognized that the incidence of acute rheumatism is in some way related to poor social and environmental conditions, and attempts have been made to determine what are the important factors and how they operate. Traditionally, living in damp houses and the influence of damp climate were considered important, but there has been little consistent evidence in support of these suppositions. That overcrowding plays a part was suggested by the experience of Dudley[1] in training ships and of Bradley[2] in a residential school, and Perry and Roberts[3] showed that the incidence of rheumatic heart disease in different wards of Bristol was highly and significantly correlated with overcrowding, as measured by the number of persons per room. Daniel,[4] in a more detailed study in the same city, confirmed this, and in addition concluded that low family income was associated with high incidence. A study of children in Glasgow and London hospitals[5] suggested that, although the disease was rare among the children of the well-to-do, the artisan class was subject to the greatest risk. Morris and Titmuss,[6] on the other hand, showed that among males aged 20–35 years in England and Wales there was a steady increase in mortality from heart disease, assumed to be principally rheumatic at this age, on descending the social scale from the Registrar-General's Social Class I, the professional occupations, to Class V, the unskilled workers, and they considered that "the whole complex of poverty" was involved. They did not consider that urbanization or overcrowding as such were important influences. Knowelden,[7] analysing mortality from heart disease at ages 15–34 years in thirty county boroughs, found a significant correlation with the proportions of the employed population in the lower social classes, but little association with overcrowding.

A major defect of many of these studies has been that they were concerned with morbidity and mortality from rheumatic heart disease and not with the incidence of the underlying condition, rheumatic fever. A factor which increases the prevalence of rheumatic heart disease might act either by increasing the frequency of attacks of rheumatic fever or by facilitating the development of heart disease in patients so attacked. Which of these two possible mechanisms is responsible cannot be determined from information on the end-result, heart disease, alone. Still further does this argument apply to studies based on heart disease mortality in which another variable, fatality from heart disease, is introduced. Since 1947, however, acute rheumatism has been notifiable in certain specified areas in England, making available for the first time routine information on the frequency of first attacks of rheumatic fever. In an analysis of these records received in the first three years of the scheme, Hewitt and Stewart[8] conclude that, though children of unskilled workers are far more commonly affected than are children of professional and skilled workers, bad housing conditions or poverty are not the responsible factors. They emphasize the greater risk of infection in large families compared with small, and in children just attaining school age compared with children of pre-school age.

The approach to the epidemiology of rheumatic fever has changed with the wider acceptance of the fundamental part played by preceding streptococcal infections. Clinical observations of epidemics of rheumatic fever following epidemics of streptococcal infection have been supplemented by studies of anti-streptolysin titres in rheumatic children, and *Streptococcus pyogenes* has been obtained from a high proportion of throat swabs in children suffering from rheumatic fever. Some trials of prophylaxis by sulphonamide or penicillin in children who have had previous attacks of rheumatic fever have shown that a reduction in streptococcal carrier and infection rates has been associated with a reduction in the incidence of recurrences,[9 10] but this has not always been confirmed.[11 12] It is suggested, therefore, that the social incidence of rheumatic fever is the direct result of the social incidence of streptococcal infection.

A recent paper based on observations in Melbourne helps to clarify the picture. Holmes and Rubbo[13] show that in the years 1938–48 the attack rate of rheumatic fever, based on hospital cases, in children living in low rental areas was three times that in high rental areas, the rate in medium rental areas occupying an intermediate position. Investigations carried out in certain schools in 1947 and 1948 revealed that the carrier rate for *Str. pyogenes* and the proportion of Dick-negative

1 *Spec. Rep. Ser. med. Res. Coun.* (*Lond.*), No. 111, 1926.
2 *Quart. J. Med.*, 1932, **25**, 79.
3 *British Medical Journal Suppl.*, 1937, **2**, 154.
4 *J. roy. statist. Soc.*, 1942, **105**, 197.
5 *Spec. Rep. Ser. med. Res. Coun.* (*Lond.*), No. 114, 1927.
6 *Lancet*, 1942, **2**, 59.
7 *Brit. J. soc. Med.*, 1949, **3**, 29.
8 Ibid., 1952, **6**, 161.
9 Massell, B. F., *et al.*, *J. Amer. med. Ass.*, 1948, **138**, 1030.
10 Rubbo, S. D., *et al.*, *Lancet*, 1949, **2**, 311.
11 Brick, M., *et al.*, *Canad. med. Ass. J.*, 1950, **63**, 255.
12 Gale, A. H., *et al.*, *Lancet*, 1952, **2**, 61.
13 *J. Hyg.* (*Lond.*), 1953, **51**, 450.
14 *Arch. Dis. Childh.*, 1948, **23**, 1.

children were both greatest in the low rental areas and least in the high rental areas. They also observed a social pattern in tonsillectomy similar to that seen by Glover in England,[14] with greatest tonsillectomy rates in the higher rental areas. Within each school the streptococcal carrier rate was considerably greater in children who still had their tonsils present than in those who had undergone tonsillectomy. The authors come to the conclusion that tonsillectomy protects against rheumatic fever by reducing the streptococcal carrier rate and also the infection rate.

Holmes and Rubbo propound an interesting theory to account for the social distribution of rheumatic fever, but they have far from proved their case. For example, to clinch their argument they observed that the tonsillectomy rate for rheumatic children, 26%, was even less than that for schoolchildren in the low rental area, 35%. However, this proportion is based on information on only 250 rheumatic children out of the total of 1,469 observed in the whole period, and the effect of this selection cannot be determined. Further, although a precise age distribution is not given, there is evidence to suggest that these rheumatic children may have been younger than the school groups investigated, and this would make any comparison of tonsillectomy rates invalid.

Epidemiology is the art of welding together evidence from many sources. The many investigations into the social incidence of rheumatic fever illustrate this by the contributions of clinical observation, of field studies, of vital statistics, and of laboratory investigation. The story, by its contradictions and uncertainties, also shows that epidemiology demands clear interpretation of precise data.

PENSIONS AND THE COMMUNITY

A great deal has been heard in recent years about the burden the growing numbers of old people will throw upon the community. For this reason an authoritative study showing that the burden can be shouldered without undue strain is reassuring. Such a study was recently undertaken by a research group of the Institute of Actuaries and the Faculty of Actuaries, whose report[1] was published last week. The problem the actuaries set themselves to examine was this. At any given period the country's national income has to maintain a certain number of people who for one reason or another are not contributing to that income —because they are too young or too old, unemployed, or sick and disabled. But in twenty-five years' time those who will have to be maintained because they are old will have increased in numbers by 50%. Not only this: they will have acquired, in the shape of pensions of all kinds, rights to consume goods and services that will have to be honoured. But if the amount of goods and services produced remains stationary, the old people's rights can be honoured only by compelling, mainly through severe taxation, the earning members of the community to consume less. If this reduction in their standard of living does not take place, if everyone is allowed to try to consume as much as before of a constant amount of goods and services, then prices will be pushed upwards and the people to suffer will be those on fixed incomes and pensions.

The best answer to this problem is a steady rise in the national income—and thus in the amount of goods and services available—large enough for the pensioners' claims on it to be met without reducing the share of others. Before the war, productivity per head is thought to have increased at the rate of 1½% per annum, and since the war there have been years when the rate was as high as 3%. If merely the lower rate is maintained over the next thirty years it will bring about, the actuaries estimate, an increase in the national income of 56%. If, in the same period, pension rights continue to grow so that everyone eventually receives a total retirement pension (including the National Insurance pension) equal to two-thirds of his average earnings, pension payments, according to the actuaries' calculations, would absorb 11% of the national income—or 14% if widows are allowed half their husbands' pensions. The estimated rise in the national income will therefore easily provide for this and for a higher standard of living for other members of the community.

The actuaries' conclusion is reassuring. But is it over-optimistic? One comment that may spring to a professional man's mind is that, even if the national income has been steadily increasing since the war, it does not seem to have improved his standard of living. A bigger national income can always be redistributed according to the fancies of the Government in power, and the heavily taxed middle-classes may well feel that they have seen precious little of the rise since the war. Are they to bear more than their fair share of the amount to be raised by taxation to meet the growing cost of State pensions—as well as any claims on the higher national income that the other social services may stake? Secondly, although it is perfectly realistic to assume that productivity per head will increase at its pre-war rate, this cannot be taken as inevitable. Since there are

[1] *The Growth of Pension Rights and Their Impact on the National Economy* 1954. London.

now virtually no unemployed resources, as there were before the war, a rise in productivity depends on more capital investment and continued technological progress. The actuaries maintain that pension schemes, by enforcing savings, will help capital investment, but they agree that they only do so indirectly. It remains to be seen whether, with all the disincentive of heavy taxation, the country's economy is flexible enough to make the constant adjustments necessary if the national income is to expand indefinitely.

The actuaries were concerned only with the burden of pensions. But old people cannot be guaranteed a certain income and then allowed to get on with it. Their health is frailer, for one thing, and they need more medical care than the younger members of the community. There is no doubt that they will throw an ever bigger burden on the National Health Service, which means that it, in its turn, will have to demand a higher share of the national income. The burden of old people cannot indeed be measured solely in money terms. They raise all sorts of problems—of where and how they should live and who should be responsible for them. The burden will have to be accepted, and the actuaries have shown that, provided there is no national disaster, the next generation of old people need not fear real poverty. But that is only the beginning.

ANTHRAX PROTECTIVE ANTIGEN

The Pasteurian method of producing active immunity against anthrax by means of a living avirulent vaccine has hitherto not been superseded in the seventy years since it was introduced. Killed vaccines are ineffective. On the other hand it is also fifty years since Bail[1] showed that the anthrax bacillus liberates a substance in the body which has an immunizing action; filtrates of fluid from the lesion were shown to have this effect. The antigen responsible was first obtained from cultures by Gladstone,[2] the medium used containing serum or serum albumin. In order to concentrate or isolate the antigen it would be preferable to cultivate the organism in a protein-free medium, and such cultivation on an extensive scale has now been highly successful in the hands of Belton and Strange[3] at the Microbiological Research Department, Porton. The medium used contained, apart from minerals and other basal constituents, certain amino-acids, a casein hydrolysate, yeast extract, and charcoal. The antigen was obtained from culture filtrates by lyophilization or alum precipitation. Satisfactory yields were given by cultures not only of a virulent but of the avirulent "Weybridge" strain. The material was non-toxic, and in small doses produced solid immunity in rabbits and monkeys against inoculation by injection and inhalation respectively with many times the minimum lethal dose of virulent organisms. Immunization of horses with the alum-precipitated antigen (length of course unstated) yielded a serum the protective power of which was at least equal to that obtained by the usual method of immunization with a living spore vaccine.

In a second paper Strange and Belton[4] describe attempts to purify the antigen. It may be true to say that large amounts of this material can be produced "with normal laboratory equipment" if normal is understood in a qualitative but not quantitative sense: 1,000 litres of culture were used per week, and the filtration system dealt with 230 litres in five hours. Alum precipitates from this filtrate were the starting material for a process of fractionation which yielded a protein, apparently the protective antigen itself, and a polysaccharide resembling that described by Ivanovics.[5] The sedimentation pattern and other properties of the protein were consistent with its being a single substance. A single dose of as little as 25μg. of a good batch gave 100% protection in rabbits against challenge with 250 average lethal doses of spores.

It is by methods of this kind, feasible only in an institution with lavish and large-scale equipment, that future progress in obtaining immunizing material of a high degree of activity is likely to be achieved. This antigen has an unexampled potency and may already have been obtained in a state approaching purity. If so, it is the first of its kind, and makes the materials used for most other forms of active immunization look very crude by comparison. There appears to be no reason why it should not replace avirulent living spore vaccines for all purposes for which they are used and for any others which may suggest themselves. The duration of the immunity produced will require further study. These workers mention only that tests on monkeys after one year showed no evidence of waning resistance.

[1] *Zbl. Bakt.*, 1904, *I Abt., Orig.*, **38**, 266.
[2] *Brit. J. exp. Path.*, 1946, **27**, 394.
[3] Ibid., 1954, **35**, 144.
[4] Ibid., 1954 **35**, 153.
[5] *Z. ImmunForsch.*, 1938, **94**, 436.

A WIDER VIEW OF EPIDEMIOLOGY

Epidemiology is usually defined as the science of epidemics, and since the term epidemic has been largely confined to the communicable diseases the uninitiated might expect the "epidemiological method" to be the technique of studying the group prevalence and incidence of infections. The term has no such restriction for Dr. John Gordon, of Harvard, who addressed the Epidemiological Section of the Royal Society of Medicine on April 30 on "The Epidemiologic Method in Modern Perspective" and hardly mentioned communicable diseases. He maintains that the techniques developed for the investigation of epidemic diseases can profitably be employed in a far wider field. Although epidemiology still has its immediate practical use as the diagnostic method of public health—its analyses and tabulations are the clinical signs on which health

officers can base diagnosis and prognosis of the mass prevalence of disease—Dr. Gordon was more concerned with its fundamental contribution to knowledge of the diseases (and also of the health) of a population.

The cause of any disease can be sought by three approaches: the clinical investigation of particular patients; the study of possible aetiological factors in the microbiological, pathological, or physiological laboratory; and the epidemiological study of the disease as it affects a number of patients and as it occurs in different geographical or social groups. The three methods of study must continuously interact. The clinician and the laboratory worker can direct attention to possible aetiological agents; and the epidemiologists in investigating them may find correlations that have little real meaning until confirmed by direct experimental study. No wonder that, as Dr. A. M. McFarlan recalled at the R.S.M. meeting, Dr. Gordon's ideal epidemiologist is one who has clinical responsibility for his patients, carries out the field as well as the laboratory investigations, and finally performs the statistical analyses. No wonder too that such an ideal individual has usually to be replaced by a team of specialists.

Dr. Gordon said little about what really constitutes the epidemiological method, and Dr. Ian Taylor's suggestion that the chief characteristic of its practitioners is an attitude of mind that can see beyond the patient in the bed still does not offer very precise guidance to the newcomer. Professor R. Cruickshank[1] gave more helpful detail in his presidential address to the Epidemiological Section two years ago. It seems that what the epidemiologists consider their method (and it differs little from what the practitioners of "social medicine" or of "preventive medicine" regard as theirs) comprises the cumulation of experience from a number of cases, and the treatment of this material by statistical methods, with particular emphasis on possible correlations with environmental or social conditions. Although the early stages of an investigation may often be based on a series of patients suffering from the disease, it is rare for one to be concluded without study of "controls," or indeed of whole population groups.

Clinicians are sometimes scornful of statisticians because their method has to be selective, and because it is not possible to describe the whole of a patient's condition in numerical terms. The epidemiologist retorts[2] that it is only by abstracting the data in this way that it is possible, physically or psychologically, to arrive at an unbiased assessment in studying the aetiology of disease. The wise epidemiologist will rarely hope that his work will give a final answer to the problems of aetiology. Dr. Gordon's[3 4] own studies on the causes of death from accidents in Massachusetts are the sort that could lead to immediate remedial methods. But more often—as with current epidemiological studies of cancer, diabetes, heart disease, congenital defects such as mongolism, and with most nutritional problems—the hope is to restrict the field within which the clinician or pathologist has to seek.

[1] *Proc. roy. Soc. Med.*, 1952, **45**, 621.
[2] Greenwood, M., *Epidemics and Crowd Diseases*, 1935, London.
[3] *Amer. J. med. Sci.*, 1949, **217**, 325.
[4] *Amer. J. publ. Hlth*, 1949, **39**, 504.

ANTIHISTAMINE DRUGS IN DERMATOLOGY

In recent years there has been a striking increase of dermatitis venenata from the use of topical applications to which the patient is sensitive: it is perhaps the most important skin disease for the practitioner to be able to recognize. Many substances of complex chemical structure have been put on the market, and the suggestion of a rational scientific purpose behind their use has made them attractive to doctor and patient. The antihistamine drugs are an outstanding example and may be assumed to have been a great commercial success. Their use has, however, been much abused. Introduced to medicine by Bovet,[1] these drugs are not the least spectacular or important of the many remarkable chemical discoveries of the last two decades. The antihistamines are of importance in experimental pharmacology and have a wide range of application in general medicine. The antihistamine effect is one common to local anaesthetics, analgesics, and the quinidine type of drug, and the antihistamines themselves share the properties of all these drugs. The range of usefulness in clinical practice may not yet have been fully explored, and it would be foolish and harmful to condemn a drug of obvious importance because of the common fault of abuse.

Because of their local anaesthetic and general sedative effects the antihistamines tend to be used for any and every itching affection of the skin and are prescribed as general sedatives internally. To apply a local anaesthetic for a local disturbance of function is as reasonable or unreasonable as to give a general anaesthetic for a more general disturbance of function. Unfortunately the local anaesthetics, and with them the antihistamines, stand high in the list of sensitizing agents, and much suffering results from the application of antihistamine drugs to the skin for the relief of itching and of eczematous dermatitis. Having become sensitized by local application, the patient will have a relapse of the dermatitis after taking antihistamine drugs by mouth and sometimes also after taking drugs of related chemical structure through cross-sensitization. The American Council on Pharmacy and Chemistry—acting upon the opinion of experienced dermatologists—has recently agreed to discontinue the acceptance of dermatological preparations of all antihistamine drugs and to omit from *New and Nonofficial Remedies* all currently accepted products in that category.[2] This decision would seem to be a wise one, for dermatological practice would lose little if the antihistamine drugs were entirely withdrawn. Though their use is not essential, they have a specific therapeutic effect in allergic urticaria when taken by mouth. Elsewhere in this issue Dr. R. P. Warin discusses the treatment of skin disorders, particularly urticaria, with antihistamine drugs

[1] Bovet, D., *Ann. pharm. franç.*, 1944, Suppl. 4.
[2] *J. Amer. med. Ass.*, 1953, **153**, 1447

administered by mouth, and he concludes that probably the only conditions of the skin which are benefited by them are those in which wealing is part of the eruption. These drugs have no other legitimate place in the treatment of skin disorders, and as local applications are better avoided altogether.

ALGAE AS FOOD

In the twentieth century man is faced by two contrasting perils. He may be burnt to cinders by a hydrogen bomb, or he may succumb to slow starvation through the overcrowding of the world by his ever-increasing progeny. It was the second of these that engaged the attention of the House of Lords last week, and several of the speakers showed their awareness of the urgent need to increase greatly the production of food. Much scope still remains for improving the production of crops and livestock in many parts of the world. Scientists have long been impressed, however, by the potentialities of the sea as a source of food. All denizens of the deep, from whales downwards, depend ultimately for their nutriments on the photosynthetic activities of microscopic algae or diatoms. Would it not be possible to forestall the whale, and to collect diatoms for direct use as human food? Viscount Samuel told their Lordships, for instance, that the blue whale, feeding on plankton alone, can in two years grow to a length of sixty feet and a weight of fifty tons. In the great extent of the oceans the whales are rather sparse, however, and it would be necessary to pass about thirty tons of sea water through a fine sieve in order to collect enough diatoms to weigh one ounce when dried.

According to H. W. Milner,[1] who has recently reviewed the subject, the artificial cultivation of diatoms seems a much more hopeful proposition. Extensive studies, which have already reached the pilot plant scale both in Britain and the U.S.A., have been made with the alga *Chlorella*. This unicellular organism is remarkable both for the rapidity of its growth and for the ease with which its chemical composition can be varied by modifications in the cultural conditions. Thus it may be made to contain 7 to 88% of its dry weight as protein, 6 to 38% as carbohydrate, and 1 to 75% as fat. Unlike most land plants it is entirely edible, without the necessity of discarding a husk or stalk. According to some accounts the taste is insipid, but others suggest a similarity to anchovy paste. Obviously the palatability will depend greatly on the methods of growth and preparation. Terrestrial plants cover the ground only for part of the year, and use only about 2% of the light falling on the area which they cover. *Chlorella* can be made to cover the ground for the whole year, and can use a much higher percentage of the available light. On the sun-lit roof of a factory at Cambridge, Mass., the organism is grown in a large polyethylene tube curved into an oval ring 160 ft. in circumference. The *Chlorella* is suspended in a culture medium containing nitrate, or some other form of combined nitrogen, and air mixed with a high proportion of carbon dioxide is forced through the system. A pump keeps the *Chlorella* moving round, and a centrifuge removes the crop when the concentration exceeds the optimum for rapid growth. A cooling system is incorporated to prevent the development of excessive heat in the culture medium.

For the manufacture of one ton of dried *Chlorella* about two tons of carbon dioxide and 1.1 tons of potassium nitrate are needed. The degree of "supercharging" to which the organism is subjected may be judged from the inclusion of 5% of carbon dioxide in the circulating air, as compared with only 0.03% in the natural atmosphere. In one year an area of one acre could provide forty tons of dried material, which when cultivated at this rapid rate would contain 50% of protein and 7% of fat. According to current estimates the price under conditions of mass production would be 25–30 cents per lb. If the yield could be doubled and the cost cut in half *Chlorella* would immediately become highly competitive with farm produce in a free market. This might well come about by the selective breeding of new strains, a point made in the House of Lords debate by Lord Stamp, who is professor of bacteriology at the Postgraduate Medical School of London. It would appear that the artificial provision of food by unicellular algae may soon leave the realms of fantasy and become solid fact.

[1] *Scientific American*, 1953, **189**, 31.

THE ANNUAL MEETING

If the programme of the Annual Meeting published in the *Supplement* this week describes the mingled fare, both grave and gay, offered to visitors, it must perforce omit from the list that unfailing ingredient of Annual Meetings—the hospitality of the hosts. As Dr. A. L. Goodall wrote last week,[1] "Perhaps the most pleasing of the commonly heard remarks of the visitor to Glasgow is that the people are amongst the kindest and most hospitable in the world," and a warm welcome awaits those many doctors who have made arrangements to attend the meeting. Those who have not yet done so would be well advised to make them soon. The plenary sessions, which have proved so popular in previous years, are to be on sleep, food and disease, and pulmonary tuberculosis, subjects of wide interest on which it is hoped many of the visitors will speak. A scientific exhibition is again to be a feature of the meeting, and here technical ingenuity comes into its own. At least one exhibit is to be so up to date that the exhibitors, who are illustrating their current research, are not sure yet what the scope of their exhibit will be. The Scientific Sections will range over clinical medicine, and many excursions have been arranged. Moreover, in the city of Glasgow and its 500-year-old university there is much to see of special interest to medical men. It was here that Lister devised his antiseptic system of surgery, and William Hunter's museum recalls to memory the genius of an earlier pioneer in our profession. The President-Elect is Sir John McNee, for seventeen years regius professor of practice of medicine at Glasgow until his retirement last October.

[1] *Supplement*, May 1, p. 20.

CLINICAL PATHOLOGY IN GENERAL PRACTICE

PITUITARY FUNCTION

BY

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Developmentally the pituitary body can be divided into two parts: that which derives from Rathke's pouch in the buccal cavity and which in the fully developed gland forms the anterior and intermediate part of the gland, and that developing from nervous tissue, represented by the posterior part. The intermediate part is vestigial in man, and its function, if any, has not been satisfactorily elucidated; it is not considered in this article. The anterior pituitary has quite different functions from those of the posterior pituitary and no reason is apparent why the two parts should be joined to form one anatomical structure.

Laboratory tests alone are not always sufficient to diagnose abnormal pituitary function. They can usually only be interpreted by a simultaneous consideration of the clinical findings. In particular a search for evidence of a space-occupying lesion in the region of the pituitary should never be omitted.

Posterior Pituitary

The posterior pituitary is connected by nervous pathways to centres in the hypothalamus, notably the supraoptic and paraventricular nuclei. Its secretory activities seem to depend upon the integrity of these pathways. Extracts of the gland have three main actions. In the first place, they cause a great diminution in urinary output, which has been shown to be due to increased reabsorption of water by the renal tubules; secondly, they cause generalized vasoconstriction and increased peristalsis of the intestine; and, thirdly, they produce contraction of the pregnant uterus. Only the antidiuretic activity is considered here.

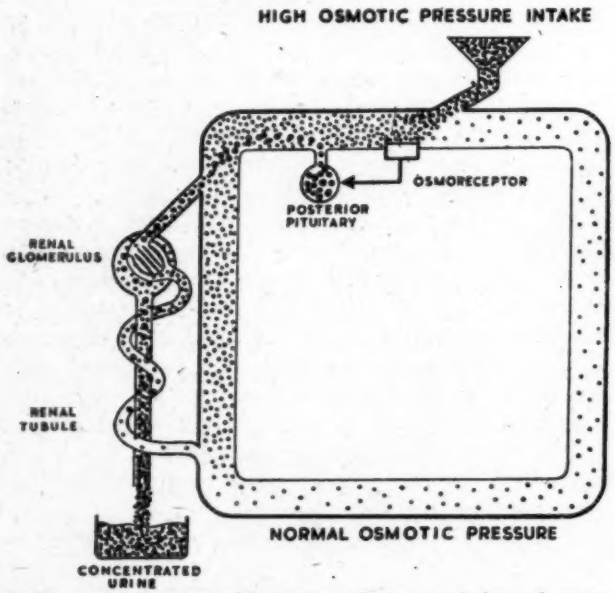


FIG. 1.—Diagrammatic illustration of the regulation of extracellular osmotic pressure by antidiuretic hormones.

It has been shown by Verney that there exist certain cells, called by him "osmoreceptors," which are probably situated in the supraoptic nucleus of the hypothalamus, and which are sensitive to changes in the osmotic pressure of extracellular fluid—in other words, to the concentration of dissolved particles. Whenever this rises above normal, nervous impulses from the osmoreceptors to the posterior pituitary result in the secretion of increased amounts of "antidiuretic hormone" (A.D.H.). This causes an increase in the amount of water reabsorbed by the distal tubules of the kidney, with the consequent production of a more concentrated urine and a fall in the osmotic pressure of extracellular fluid. The system is represented diagrammatically in Fig. 1.

In contrast to the above, lack of secretion of the posterior pituitary will result in the passage of large quantities of very dilute urine and consequently in intense thirst. This is the syndrome of diabetes insipidus.

Diagnosis of Diabetes Insipidus

Clinically, deficiency of posterior pituitary secretion should be suspected whenever a patient complains of intense thirst and polyuria, and when it is found that the urinary specific gravity is never above 1005. Differentiation from diabetes mellitus should present no difficulty because of the presence of glycosuria and a high urinary specific gravity in this condition. In chronic nephritis there are proteinuria, a specific gravity of the urine fixed at about 1010, and a raised blood urea. There are, however, two conditions which can only be differentiated from posterior pituitary deficiency with more difficulty—namely, nephrogenic diabetes insipidus and polydypsia of psychological origin. The first of these two conditions is a rare familial disorder in which the renal tubules do not appear to respond to A.D.H. Differentiation can be made by the following test.

At some specified time—for example, 8 a.m.—the patient is instructed to empty his bladder and the urine obtained is discarded. Any urine passed during the next hour is placed in a bottle labelled "8 a.m. to 9 a.m." At 9 a.m. the bladder is again emptied and the urine placed in this first bottle. Another bottle labelled "9 a.m. to 10 a.m." is provided for urine passed during the second hour, and at 10 a.m. the bladder is emptied into this bottle. Pitressin, at a dosage level of 0.1 unit per 1 kg. body weight, is given subcutaneously at this time. Two further one-hourly samples of urine are obtained in the same manner as the others. The specific gravity and the volume of each of these samples is measured. There should be no restriction of water during this test unless a considerable fall in urinary output after the injection of pitressin is found; in this event, large quantities of water should not be taken until the urinary volume increases. In normal subjects who have not been on restricted fluids, in patients with true diabetes insipidus, and in those with psychological polydypsia the injection of pitressin will be followed by a considerable diminution in the rate of urinary secretion (to less than 1 ml. a minute) and by a marked increase in the specific gravity of the urine. No such change will be found in those with nephrogenic diabetes insipidus.

The following test will differentiate true diabetes insipidus from psychological polydypsia. It should only be carried out with the patient under carefully controlled conditions, otherwise the interpretation may not be satisfactory, and, furthermore, the patient may become seriously dehydrated.

Water is allowed freely, and, there being no evidence of dehydration, two one-hourly samples of urine are collected as in the above test. Water and food are then completely withheld for the next six hours and urine is collected during this period in one-hour samples. In normal subjects and in those with psychological polydypsia the specific gravity of the urine will increase considerably during the water deprivation (to above 1010) and its volume will fall. In those with true diabetes insipidus, however, and in those with nephrogenic diabetes insipidus there will be little change in the urinary specific gravity and volume.

A further test, proposed by Lewis and Chalmers, depends upon the observation that nicotine will stimulate the production of A.D.H.

Urine is collected at 10-minute intervals, and if the urinary flow does not exceed 10 ml. a minute the patient is instructed to drink more water until this level is reached during two consecutive intervals. Cigarettes are then smoked and the smoke inhaled until severe malaise or nausea and perhaps vomiting occurs (this may require up to three cigarettes), the urine being continuously collected at 10-minute intervals. In normal subjects and in those with polydypsia of psychological origin there will be a considerable diminution in urine flow and a rise in urinary specific gravity. There will be little or no effect in patients with true diabetes insipidus, nor presumably in those with nephrogenic diabetes insipidus.

Occasionally a patient with diabetes insipidus will have only a partial lesion of the A.D.H. mechanism, and in this event all these tests may have rather equivocal results.

Anterior Pituitary

On the basis of staining reactions there are three types of cells in the anterior pituitary—basophil cells, which stain with basic dyes; acidophil cells, which stain with acid dyes; and chromophobe cells, which do not stain readily at all. There is no definite evidence that the chromophobe cells secrete any hormone; it seems more likely that they are early forms of both acidophil and basophil cells.

The acidophil cells probably produce a hormone which has been called pituitary growth hormone or somatotrophic hormone (S.T.H.); and hyperplasia or a tumour of the eosinophil cells, producing excessive quantities of this hormone, gives rise to the clinical picture of gigantism or of acromegaly; conversely, lack of this hormone contributes to the picture of pituitary dwarfism. There is a considerable amount of evidence that S.T.H. is very closely allied to, if not identical with, the pituitary substance which will produce diabetes mellitus (diabetogenic hormone).

The basophil cells probably secrete many different hormones, and these seem mainly to control the activity of other endocrine glands. Because of the action of this group of hormones the pituitary has been called the "leader of the endocrine orchestra." They are (1) thyrotrophic or thyroid stimulating hormone (T.S.H.); (2) the hormone which stimulates the adrenal cortex (A.C.T.H.); (3) a substance which stimulates ovarian follicles in the female and the seminiferous tubules in the male (F.S.H.); (4) interstitial cell stimulating hormone (I.C.S.H.) or luteinizing (L.H.); (5) lactogenic hormone — prolactin, which is probably identical with luteotrophic hormone (L.T.H.); Nos. 3, 4, and 5 are collectively termed the gonadotrophins. It seems certain that the output of these hormones is controlled, possibly through chemical mediators, by centres in the hypothalamus. In addition, in the case of T.S.H. and A.C.T.H. the output of these substances is suppressed by thyroid hormone and by the steroids derived from the adrenal cortex, respectively. This system of control is very important and is represented by the pituitary–thyroid relationship (the so-called pituitary–thyroid axis) in Fig. 2.

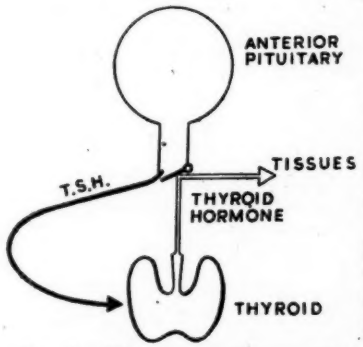


FIG. 2.—Diagram to illustrate the internal regulating arrangements of the pituitary–thyroid axis

It will be seen that externally administered thyroid hormone, provided the dosage is within the controlling limits of the system, will not result in any increase in thyroid hormone in the body, since there will be a suppression of T.S.H. and a diminished output of endogenous thyroid hormone. Similarly, when cortisone is given there is a suppression of A.C.T.H. production, with consequent diminution in the activity of the adrenal cortex. This is very important, since, if cortisone which has been given therapeutically is suddenly discontinued, there is a period before the resumption of endogenous production of A.C.T.H. and consequent stimulation of increased adrenocortical activity when the patient may suffer from acute insufficiency of adrenocortical activity and may die as the result of what would normally be trivial trauma.

F.S.H. in the female stimulates the development of follicles in the ovaries, and, in conjunction with further stimulation by L.H., oestrogens are produced and maturation of the follicle with ovulation and the formation of a corpus luteum occurs. Further stimulation with prolactin or L.T.H. maintains the corpus luteum for about two weeks and results in progesterone formation. It seems probable that the oestrogens inhibit F.S.H. and stimulate L.H. production, and that, by contrast, progesterone stimulates F.S.H. and inhibits L.H. production. In addition to its action on the ovary L.T.H. will initiate lactation in mammary glands which have undergone the appropriate development associated with pregnancy.

In the male the relationship of these gonadotrophic hormones is by no means so clear, but it seems that F.S.H. stimulates the development of the seminiferous tubules, and that L.H. stimulates the Leydig cells, which, as a result, secrete androgens or masculinizing hormones.

Assessment of Anterior Pituitary Function

It can be seen from the foregoing that *direct estimations of the hormones of the anterior pituitary would by themselves give no precise information about whether there was a primary pituitary disorder or not.* There are, in any case, no methods of assay of these hormones available for general routine clinical use, though estimations of some are carried out in certain centres. Gonadotrophins are measured in the various tests for pregnancy, but these are derived from the placenta and are present in very much greater quantities than pituitary gonadotrophins.

Tumours of one type of anterior pituitary cell may either stimulate or depress the activity of the other cells. Thus chromophobe tumours, which in themselves have no secretory activity, usually cause a diminution in anterior pituitary function; on the other hand, eosinophil adenomas may be associated with evidence of increased or of decreased activity of the basophil cells.

Thus pituitary abnormalities must be assessed on clinical grounds and by tests of function of those peripheral endocrine glands which are under pituitary control.

On Clinical Grounds

1. By neurological and radiological evidence of a space-occupying lesion in the region of the pituitary. Such a lesion should always be looked for, although of course it is often absent.

2. By a preceding history of an obstetrical catastrophe or intense shock from haemorrhage, followed by symptoms and signs suggestive of deficient pituitary function resulting, as shown by Sheehan, from necrosis in the anterior pituitary.

3. By inference from a combination of clinical signs of various endocrine disturbances—for example, gain or loss of weight, failure of lactation, amenorrhoea, feeling of the cold, loss of libido, loss of axillary and body hair, and atrophic vaginal mucosa on the one hand, and acromegaly, masculinization, Cushing's syndrome, hirsutism, etc., on the other.

4. In childhood, by a consideration of the development of puberty, of growth rate, and of the appearance and union of epiphyses, all taken in conjunction with the patient's age.

By Tests of Function of Peripheral Endocrine Glands under Pituitary Control

The Adrenal Cortex*

(*a*) *Urinary 17-Ketosteroid Excretion.*—The most direct test of adrenocortical activity in common use is the estimation of the daily output of 17-ketosteroids in the urine. These substances, which stimulate the laying-down of body protein and which may also induce masculinization, are produced both by the adrenal cortex and by the interstitial cells of the testis. The whole of the urinary output in the female is thus derived from adrenal activity, whereas in the male about two-thirds of the total is derived from the adrenals and the remainder from the testes.

A quantitative 24-hour collection of urine is made and 10 ml. of concentrated hydrochloric acid is added as a preservative. This is assayed chemically for 17-ketosteroids; the normal output for 24 hours is roughly as follows, but the figures vary slightly in different laboratories: Adult males, 8 to 22 mg.; adult females, 5 to 14 mg.; children under 8 years, below 1 mg.; subjects between 8 and 20 years a gradual rise to the adult levels of the appropriate sex. In the female, values lower than the above indicate deficient secretion by the adrenal cortex. In the male, low values also usually indicate deficient function of the adrenal cortex (since this produces the major part of the 17-ketosteroids); deficient interstitial testicular secretion may result in somewhat low figures, though often they are in the normal range. If 17-ketosteroids are very low (absent or almost so) then it is probable that both the adrenal cortices and the testes are deficient and this will almost certainly result from anterior pituitary deficiency. Deficient secretion of adrenal 17-ketosteroids in both male and female may be due to a primary abnormality of the adrenal cortex or it may be secondary to anterior pituitary dysfunction. These can be differentiated by finding out whether 17-ketosteroid output varies after several days of treatment with A.C.T.H.—for example, 25 I.U. six-hourly (see below).

Increased amounts of 17-ketosteroids may result from increased stimulating activity of the anterior pituitary or from tumours of adrenal or testicular tissue.

(*b*) *Estimation of 11-Oxysteroids in the Plasma or Urine.*—These are the hormones secreted by the adrenal cortex, which are concerned in carbohydrate metabolism and in protecting the body against the non-specific effects of injury; cortisone and hydrocortisone are members of this group. Adequate routine methods for the estimation of these substances in plasma are not generally available, but when they do become so they will be extremely important and valuable. Routine methods for urine are in existence, the urine being collected quantitatively for 24 hours, as for the 17-ketosteroids. It will be appreciated, however, that these urinary substances are largely metabolic end-products and an exact interpretation of the findings is still not possible.

(*c*) *Adrenal Response to A.C.T.H.*—A final diagnosis between pituitary deficiency and adrenal cortex deficiency can be made by following the effect of injections of A.C.T.H. upon 17-ketosteroid output. Obviously, if there is no functioning adrenocortical tissue, there will be no increase in 17-ketosteroid output when A.C.T.H. is given. By contrast, when the lesion is one of the anterior pituitary, the injection of A.C.T.H. will, after an interval, result in an increased secretion of 17-ketosteroids. Details of this test vary in different centres; the one I use is as follows:

Twenty-four hour samples of urine are collected from 6 a.m. to 6 a.m. on each of two control days when no A.C.T.H. is given, and the 17-ketosteroid content of each is estimated. At 10 a.m. and 4 p.m. on each of these days blood is taken and the number of eosinophils per c.mm. is estimated. Starting at 6 a.m. 25 I.U. of A.C.T.H is then given intramuscularly every six hours for four to seven days. On each of these days the 24-hour output of 17-ketosteroids is determined, and also at 10 a.m. and 4 p.m. blood is taken for enumeration of the eosinophils.

When there is insufficiency of the adrenal cortex—for example, in Addison's disease—there is no change in the urinary output of 17-ketosteroids and no change in circulating eosinophils. By contrast, when there is diminished function of the anterior pituitary, the output rises, usually on the second day of A.C.T.H., and even more on the third and fourth days; at the same time there is a fall in the number of circulating eosinophils and these are usually absent by the end of the third day. In cases of marked pituitary deficiency of long standing it may take five or six days before a significant response is obtained. The eosinophils are counted, because it has been found that the number of these cells per c.mm. of blood is decreased by 11-oxysteroids, and a decrease in their numbers forms a convenient index of increased secretion of these hormones.

(*d*) *Tests Associated with the Electrolyte- and Water-Regulating Effect of the Adrenal Cortex.*—The water diuresis test presupposes that there is no abnormality of renal function and no liver disease. The patient drinks 1.5 litres of water in the course of 15 minutes, and the excretion of urine hour by hour is recorded. Normally, over 1,000 ml. should be secreted within five hours. With decreased activity of the anterior pituitary and with primary lack of function of the adrenal cortex there is only a small diuresis or none at all during the five-hour period. If the test is repeated on the fifth or sixth day of A.C.T.H. therapy at a dosage of 25 I.U. intramuscularly six-hourly a normal response will be obtained if there is primary pituitary deficiency; in primary adrenal deficiency water diuresis will remain deficient.

(*e*) *Tests of Carbohydrate Metabolism.*—A glucose-tolerance test carried out in the usual way shows a flatter curve than normal in hypopituitarism. In acromegaly and in other syndromes resulting from increased activity of the anterior pituitary the curve is often diabetic in type, in the former because of the diabetogenic effect of S.T.H. and in the latter because of associated overactivity of the adrenal cortex. An insulin-tolerance test carried out by following the change in blood sugar at 30-minute intervals following the intravenous injection of 0.1 unit of insulin per kg. body weight shows an abnormal degree and an abnormally prolonged period of hypoglycaemia in hypopituitarism, whereas in increased pituitary activity there may be no fall in the blood-glucose level. Care should be taken when this test is performed, since in hypopituitarism there is a risk of profound and possibly irreversible hypoglycaemia.

The Thyroid†

Thyroid function is estimated by the basal metabolic rate or by the uptake of radioactive iodine. These may show deficient function either in hypopituitarism or in primary lack of thyroid function. It is possible to stimulate thyroid activity by injections of T.S.H., and this can be used for differentiation. However, no test of this type is yet in general use.

The Gonads‡

In the female the lack of oestrogen production which accompanies hypopituitarism may be detected by the appearance of the cells in smears from the vaginal mucosa.

A small amount of vaginal secretion is aspirated into a glass tube by means of a rubber bulb. In hypopituitarism the vaginal mucosa is characteristically free from secretion and it may be very difficult to get material for a smear. However, if anything is obtained it is then spread thinly on to a clean microscope slide which is *immediately* plunged into a mixture of equal parts of ether and ethyl alcohol for fixing. It is of great importance that the smear should not dry before being plunged into the fixative, since this results in distortion of the cells and in alteration of their staining

*See also Dr. F. T. G. Prunty's article on "The Assessment of Adrenal Cortical Activity" (March 27, p. 751).

†See also Dr. Russell Fraser's article on "Tests of Thyroid Function" (March 20, p. 696).

‡See also Dr. G. I. M. Swyer's article on "The Assessment of Gonadal Function" (April 10, p. 866).

reactions. After fixation for at least two hours the slide can be posted, if necessary, to a suitable laboratory for staining and interpretation, but it is probably preferable to keep it in the fixing solution. It is stained with the special stain devised either by Papanicolaou or by Shorr. Interpretation should be attempted only by someone thoroughly conversant with the technique.

The chemical estimation of oestrogens in the urine is difficult and not usually necessary in the diagnosis of hypopituitarism.

In the male, testicular biopsy is sometimes used to differentiate diminution in function resulting from decreased activity of the anterior pituitary from that due to some primary testicular disorder. It is a very simple procedure and can be carried out under local analgesia. It is only occasionally necessary, and if F.S.H. estimation can be carried out will usually be unnecessary, since with primary pituitary deficiency F.S.H. output will be absent or low, whereas it will be abnormally high with primary testicular deficiency.

Conclusion

It can be seen that there is no simple test which can be applied to determine whether the anterior pituitary is functioning normally or not. Most of the tests are indirect and non-specific, pituitary function merely being inferred from their results. Such inferences cannot usually be made on the basis of one test alone, more information, either clinical or from other tests, being required. For this reason the diagnosis of anterior pituitary dysfunction can be made only by a consideration of the clinical data, taken in conjunction with the results of one or more of the tests outlined above.

Next article on Clinical Pathology.—"Interpretation of Electrolyte Changes in the Blood," by Dr. Paul Fourman.

Refresher Course Book.—The first collection of articles in the Refresher Course for General Practitioners (fully revised) is available as a book containing 55 chapters, price 25s. Copies can be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers.

ROYAL SANITARY INSTITUTE CONGRESS

THE IMPORTANCE OF PREVENTIVE MEDICINE

The annual congress of the Royal Sanitary Institute was held at Scarborough from April 27 to 30. The attendance was reckoned at about 2,000, and included representatives from more than a thousand local authorities. The EARL OF FEVERSHAM, in his inaugural address as president, acclaimed the achievements of the National Health Service, which, he said, had now silenced frivolous criticisms even among the most prejudiced. At the same time he drew attention to some perils. Centralization of the hospital services had brought about a separation between preventive and curative sections of the public service, and this, unless it was checked, might deteriorate into a divorce. The great service of voluntary effort which used to centre around the hospital was also in danger of being lost. He urged that there was a great opportunity at this stage to strengthen the links between the work of hospital boards and medical officers of health by a greater concentration on preventive medicine.

The Public Health Team

The Congress met in ten sections, and there were four special conferences for workers in the public health field. Presiding over the Section of Preventive Medicine, Sir ALLEN DALEY said that the preventive services must do all in their power to make the curative services redundant, as had already been largely done in those fields which were first subjected to direct attack. For example, fever hospitals were now largely available for other hospital purposes, and tuberculosis of bones and joints had become a rare disease. But the burden of ill-health was still very heavy. Typhoid fever might appear again, as it did in Croydon some years ago; smallpox might slip through the barrier; apathy might develop about immunization against diphtheria, and new diseases might appear, or old ones, like poliomyelitis and hepatitis, might become more prevalent.

Dr. HENRY VAUGHAN, former Health Commissioner of Detroit, and now Dean of the School of Public Health, University of Michigan, described the steps taken in his country to train non-medical workers for the public health team, and pointed out the need for harmonious working on the part of all concerned, down to the least experienced technical assistant.

General Practitioners and Research

The relations between general practitioners and medical officers of local authorities were declared by Dr. HUGH PAUL, M.O.H., Smethwick, to be steadily growing more cordial. Much of the work of each was now dovetailed into the work of the other. The recent inauguration of the College of General Practitioners was noteworthy from the public health point of view, and even in its infancy the new College was showing a deep and intelligent interest in research. Could not medical officers of health harness its activity to their own, and by team-work find out much more of the real causes of disease? Many general practitioners were both eager and competent to carry out research work in this field, and could be enormously helped by the staff of the health departments. What about the study of diabetes? The medical officer of health might find out from the practitioners in his area a few who would co-operate in a study of the sociology of the disease.

"The family doctor is in a unique position to know the intimate family history of his patients, and a small committee of family doctors and public health medical officers, guided perhaps by a bio-statistician, could, in the course of time, bring together a mass of useful information which might well have a bearing on the causation, the course, and the prevention of the disease."

Again, the social pathology of peptic ulcer was another urgent problem, and here the team would include the hospital, with a health visitor to follow through her inquiries in the home and in the hospital and in the home again after discharge.

Spectacular successes, Dr. Paul added, must no longer be expected. "We no longer can hope to save hundreds of lives by removing the village pump handle." Future success would be hardly won, by lengthy processes and organized team-work.

Flaws in the Health Service

Dr. C. METCALFE BROWN, in presiding over the Conference of Medical Officers of Health, took as his main subject the administration and cost of the Health Service. Nearly all responsible people, he said, rightly supported the principle of a National Health Service, but forthright criticism was needed to secure necessary adjustments. It was no comfort to a patient to be assured that poverty was no bar to a hospital bed if he found, as many did, that no hospital bed was free for him within a reasonable time. In the future administration of hospitals there was a choice between the English voluntary hospital system of employing lay administrative officers and the local government and Scottish voluntary hospital system of relying on medical superintendent administration. Gradually, slowly at first but rapidly recently, it had become apparent to most people actively concerned with hospitals that the medical superintendent was indispensable, not only for smoothing interdepartmental relations but for the protection and assistance of the patient and his family.

Strong criticism had been levelled by many knowledgeable people at the regional hospital boards on the grounds that they are unwieldy, remote, soulless, inefficient, and uneconomical. It had to be faced that the hospital service

was in general no better than it was before 1948 and the cost had increased fantastically. General practitioners and public health officers in many areas had to deal daily with patients needing hospital accommodation for whom beds were not available. A multiplicity of meetings of a variety of committees were nowadays necessary for action which formerly would have been taken simply and swiftly by a local government medical officer. Administrative dynamite was required to bring about what in bygone but recent years was achieved by friendly official letters or even telephone conversations. The only remedy was to entrust hospital administration to local health authorities. Regional arrangements for consultants would still be necessary, but that could be achieved, as it had been before in some areas, by means of Hospital Joint Advisory Boards.

Examining the rising cost of the Health Service, Dr. Metcalfe Brown said that the general-practitioner service was in the main well administered, and it was not the general practitioners' fault that far too many and far too expensive drugs were absorbed by their patients. "Some contributors to the National Insurance Scheme believe they were promised and entitled to the medical earth, and they intend to get it." The public health service offered no scope for economies, as it had always been conducted on the basis of obtaining the best value for money spent. The hospital service provided the only field for far-reaching economies. There appeared to be no limit to the huge cost of the hospital service, he said, and it was difficult to see what remedy could be applied so long as the extraordinary system persisted under which policy and costs were determined by people who had no direct responsibility to the taxpayer and ratepayer. There must be a balance struck between demands for treatment and its cost, and the local authorities in whose councils the voice of the local elector was heard were the best equipped for settling this delicate problem.

Dr. Metcalfe Brown concluded his address with some brief references to research and other activities in the public health field.

Epidemiological Aspects of Poliomyelitis

The discussion at the Conference of Medical Officers of Health was on poliomyelitis, Dr. W. H. BRADLEY discussing the epidemiological aspect and Dr. J. STEVENSON LOGAN the application of present epidemiological concepts to the management of outbreaks. The latter said that in his area (Southend-on-Sea), since the beginning of July, 1952, the incidence of confirmed disease had been 1 per 1,000 of population. A few years ago it could have been said with confidence that no path of infection had been traced and that multiple cases in the same household were unknown. In 1947 a tendency to some geographical grouping of cases was noticed, and it was considered worthy of comment that an adult should develop the disease eight days after its onset in a child living next door. From that time the distribution pattern seemed progressively to become a little clearer, but it was not until 1952 that school and district spread and multiple cases in the same households were seen.

As a result of his experience Dr. Logan said that an obvious first step in prevention was the exclusion from schools and nurseries of household contacts and other children who had been in close and regular association with a notified case of poliomyelitis. Three weeks' exclusion was probably the best general rule, a period which might with advantage be extended in specific cases where there had been vague illness in the immediate environment of a notified case. It was also reasonable to exclude from their occupations all those whose work brought them into regular and sustained contact with young children. These included school-teachers and other school employees and nursery nurses and nursery attendants. At one time he had taken less stringent action with adults in these employments, but the events of 1952 had led him to alter his views. In the infected school all unnecessary re-groupings of children were clearly to be avoided. Playtime recesses should be "staggered" for different classes, and among younger children particularly the volume of organized physical activity ordinarily included in the curriculum should be reduced.

The Disabled Child

A symposium on the disabled child, in the Section of Maternal and Child Health, was preceded by an address by Professor A. G. WATKINS, the President of the Section, on the way in which the medical schools and hospitals of the country had entered the field of preventive paediatrics. During the last ten years the schools and hospitals had broadened their outlook a great deal and the study of the healthy child had been brought within their province. Infant mortality had fallen steadily, methods of immunization had improved, preventive measures had become almost routine, and the chronic illnesses of childhood had almost disappeared.

Dr. A. R. SOUTHWOOD, Director-General of Public Health, South Australia, gave an account of Australian ways with handicapped children. Much valuable work was being done by both official and voluntary bodies, but more could be achieved with better co-ordination, and it was in that direction that progress was being made. Dr. J. D. KERSHAW, M.O.H., Colchester, made some constructive criticism of the special schools for handicapped children. The special school took the child out of the social *milieu* in which he had been brought up and to which he would have to return. There should be no prejudice either in favour of the special school or against it, and the decision should be made in each case on its merits. Moreover, no school placement should be final. Dr. JEAN PARKER gave an account of what is being done in Sheffield for the disabled child, especially in occupation centres for mental defectives.

Prevention in the Mental Health Field

Three important addresses were given in a symposium on problems of prevention in the mental health field. Dr. J. A. FRASER, M.O.H., North Riding, speaking from the point of view of the medical officer of a local health authority, urged that such authorities should have restored to them the powers to house defectives in residential accommodation instead of having to rely on regional hospital boards to provide so-called "hospitals." These were, he said, in the main simply hostels for defectives where no real medical treatment was carried out. Professor T. FERGUSON RODGER dealt with the relationship between social change and the prevalence of mental illness and posed certain questions which might be taken into account in any survey:

Is the speed of social change a factor in explaining the increased prevalence of mental and nervous illness?

Is the increase in psychiatric illness related to the fact that people move about the country far more than formerly?

Is mental illness more common among those who have to live in an alien culture?

Is psychiatric disorder less frequent among those who have been brought up in and remained attached to religious belief?

What effect has the economic status of a family on the probability of one of its members succumbing to mental disorder?

Dr. J. A. HADFIELD discussed the principles of parenthood in relation to mental health and made the suggestion that homes should be established where children to the number of twelve to fifteen in separate houses could be placed under house mothers. In such homes the ordinary behaviour and disorders of children could be observed and studied by one or two whole-time trained psychiatrists who would work out the natural phases of maturation and reactions to varying types of treatment. These homes would not only be research stations but training schools, where medical officers, health visitors, and others could have experience in the handling of children.

A wide range of subjects was discussed in other sections of the Congress, including housing technique as affected by modern science, hospital planning, port health, rural

sewerage, health education, animal sources of food infection, polluted watercress beds, food hygiene and preparation, and the problems of young people during the transition from schoolchild to adult worker.

IMPERIAL CANCER RESEARCH FUND

The annual general meeting of the governors of the Imperial Cancer Research Fund was held at the Royal College of Surgeons on April 29. Professor H. R. Dean, chairman of the council, said that two years had passed since the Fund celebrated its jubilee, and during those two years much had happened. The Fund was formed in 1902, when the first director of the laboratory, Dr. Bashford, formulated a scheme for an inquiry into the nature, cause, prevention, and treatment of cancer. The Fund's laboratory was one of the first to be established for the study of cancer, and during the years it had made many contributions to knowledge. In the last century the knowledge of cancer was almost limited to its appearance in human beings, but with the new century and the work of their laboratory it had been recognized that cancer occurred frequently among many varieties of animals, that it could be transmitted by grafting from one animal to another, and that cancer could actually be initiated by chemical substances, by ultramicroscopic viruses, and other means. Cancer thus became a branch of experimental biology.

New Laboratories in Lincoln's Inn Fields

It was for these long-term investigations that their laboratories at Mill Hill existed, and a report on the work above the name of Dr. James Craigie, F.R.S., director of the central laboratories, was before the governors. In 1951, Professor Dean continued, the council made a very important decision. At its request the Royal College of Surgeons provided two laboratories in Lincoln's Inn Fields, especially for the investigation of problems concerning cancer in human beings. These were under the general direction of Professor Geoffrey Hadfield. The council decided that larger premises were necessary, and once more a request had been made to the Royal College, which promptly helped them by giving them a ten years' lease of No. 48, Lincoln's Inn Fields. This house had been adapted as a laboratory for the clinico-pathological research unit, and here a number of new appointments had been made, including a senior and two junior biochemists and a junior research pathologist. A consultant service in diagnostic cytology would in the course of the year be set up at No. 47, Lincoln's Inn Fields, which had also been leased from the Royal College of Surgeons. Still other problems were coming forward for investigation, and it was hoped that it might be possible to increase the facilities for long-term investigation. It was essential that this work should be carried on in Central London, within easy reach of the great London hospitals; and here Professor Dean thanked the surgeons and pathologists of the London hospitals for their ready co-operation.

Current Research

Professor Dean went on to refer to certain investigations which are set out in more detail in the annual report.* Dr. Craigie had been concerned in an investigation to discover how tumour cells managed to survive freezing and thawing. A special refrigerating unit had been installed for the preservation of experimental tumours, and this had facilitated certain kinds of work for which transplantable tumours of animals were required. Tumour material kept in a frozen state for nearly five years had shown a remarkable degree of survival. The ability to survive in the frozen state was not, of course, peculiar to cancer, but was shared by various normal mammalian cells. Dr. A. M. Begg had started research on the induction of lung cancer in mice following the introduction of carcinogens by the respiratory route, and Mr. H. G. Crabtree had extended his investigations, previously reported, on chemical carcinogens. Certain azo-compounds which yield sulphanilamide on metabolic breakdown were found to delay the development of butter-yellow liver tumours in rats by 6–7 weeks. Dr. L. M. Franks had carried out an inquiry into cancer of the prostate, especially from the point of view of two neglected factors, old age and the adrenal cortex, using hamsters, which aged rapidly, and guinea-pigs, which had an exceptionally large adrenal gland. Drs. G. Lumb and J. Stretton Young had been working on the morbid histology of established breast cancer. Much other work of a miscellaneous nature had gone forward.

Mr. A. Dickson Wright, Hon. Treasurer of the Fund, presented a financial statement, showing that the total receipts from investments, contributions, and other sources amounted to just over £60,000, a slight increase on the previous year's figure. This year, for the first time, legacies not exceeding £1,000 had been credited to revenue, bringing in a further sum of over £30,000. The Fund was in the happy position of being able to point to the very high proportion of expenditure incurred in its research work and the care of its laboratory buildings. Of the £91,000 income, only £4,517 was spent on administration and £6,739 on publicity.

Viscount Halifax was re-elected President and Mr. Dickson Wright treasurer.

*Imperial Cancer Research Fund: Fifty-first Annual Report, 1953–4.

PROBLEMS OF THE RHEUMATIC DISEASES

SEVENTEENTH MEETING OF EMPIRE COUNCIL

The 17th annual meeting of the Empire Rheumatism Council was held at the Royal College of Surgeons on April 28, Dr. W. S. C. COPEMAN, chairman of the Executive Committee, presiding. A message was read from H.R.H. the Duke of Gloucester, the President, in which he spoke of his pleasure on learning that the Council had initiated and was financing the first Chair of Rheumatology to be established in the Commonwealth, and that Dr. J. H. Kellgren, a member of the Council, had been appointed to the professorship.

First British Chair of Rheumatology

Dr. Copeman, presenting the annual report, said that this chair—perhaps the most important development in the whole orbit of rheumatology since the Council was formed in 1936—had been established in the University of Manchester. It was in fact only the third such chair in the world, the other two being in France and in Holland. It was an important and far-reaching accomplishment, and they all had the utmost confidence in Professor Kellgren. Another event of the year had been the invitation received by the Council to submit evidence to the committee of inquiry (the Piercy Committee) of the Ministry of Labour and National Service into the provision for the rehabilitation, training, and settlement of disabled persons. A person much overlooked and ignored in considering the problems of rehabilitation was the chronic arthritic, especially the arthritic housewife, whose return to a normal way of life was one of the most rewarding, though not one of the most dramatic, concerns of modern medicine. The securing of ministerial recognition of rheumatology as a specialty within general medicine and the institution of registrarships in rheumatology in its own right had been pursued, and it was hoped that the Minister would shortly receive another deputation on the subject, when final approval would be given to proposals on these lines.

Mr. W. R. C. HALPIN, chairman of the Finance Committee, presented a report which showed that the net income for the year (exclusive of legacies) was just over £10,000; the decrease of £3,434 on the previous year was accounted for almost wholly by a decrease in donations. Medical expenditure amounted to £8,127. The Finance Committee was very anxious to increase expenditure on research projects of merit, but could do no more than funds permitted.

Dr. Copeman was re-elected chairman, and Lord Webb-Johnson vice-chairman. The hon. medical secretary (Dr. Oswald Savage), his deputy (Dr. R. M. Mason), and the parliamentary representative (Sir Hugh Linstead, M.P.) were all re-elected, together with the various committees. The meeting closed with a vote of thanks to Dr. Copeman, proposed by Mr. C. G. Izard, seconded by Dr. Dudley Hart.

Clinical Research

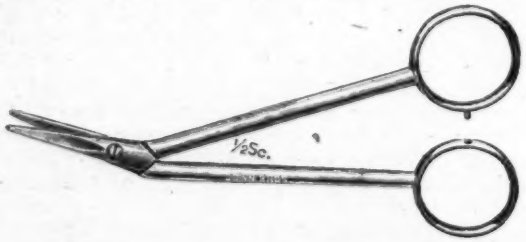
The annual report, which was adopted at the meeting, stated that certain work on steroid metabolism, including clinical trials of A.C.T.H., cortisone, and other steroid substances, at the Council's "Maclean" laboratory at the Hospital of St. John and St. Elizabeth, had terminated last year with the appointment of Dr. A. A. Henly to another position, but the Council's laboratory was not to be left without a successor and would continue to be used by an Empire Rheumatism Fellow for research work, for which new equipment and apparatus were now being obtained. Two clinical trials were in progress in which a number of hospitals were participating. One was to assess the value of cortisone and aspirin, and the other that of "hydrocortone." The report contained an account of completed and current researches under the Council's Fellowships. Two Fellowships had been recently instituted for specific research problems. Under one of these work had been undertaken at Sheffield on the oxidation of corticosteroids with sodium bismuthate, and had led to the development of an analytical method for the simultaneous determination of formaldehydogenic and 17-ketogenic steroids, and a routine procedure for the estimation of 17-ketogenic steroids in urine. Under the other, at St. Mary's Hospital, the examination of some enzymological aspects of connective-tissue metabolism was being conducted. Some basic research into the long-term treatment of rheumatoid arthritis, undertaken under the "Philip Gray" Fellowship, would shortly be published.

Preparations and Appliances

AN IMPROVED TYPE OF CORONARY SCISSORS

Dr. GEOFFREY SHERA, of Eastbourne, writes: The conventional type of coronary scissors has many faults: a clumsy, blunted tip unsuitable for very narrow coronary vessels and likely to disturb a small clot; the loops are too small for the average gloved hand; leverage is feeble; and the absence of any "angling" tends to tear a brittle vessel.

The new pattern illustrated here attempts to meet these defects. The tip is only just blunted, without increasing



its size. The loops are now adequate and eminently comfortable. Overriding is prevented by a "pin and socket" stop when strong pressure is required, and leverage is both powerful and effective. The "angling" allows the coronary vessels to be cut with the blade strictly in line with the lumen, and this ensures rapid and easy exposure thereof. One is much less likely to disturb a coronary clot with these scissors, and calcified vessels present no trouble owing to powerful leverage.

I am indebted to Messrs. Down Bros. and Mayer & Phelps, 32–34, New Cavendish Street, London, W.1, for their skill in executing the manufacture to my design.

Reports of Societies

Devon and Exeter Medico-Chirurgical Society

At a meeting on March 18 the president, Mr. Norman Capener, spoke of "The Hunterian Influence in Exeter," relating his talk to the development of a medical school there which had flourished during the first half of the nineteenth century. The school failed to survive the Medical Act of 1858, but while it lasted it had included amongst its teachers some outstanding figures. Dr. John Sheldon, F.R.S., had spent his last twenty years in Exeter, having retired owing to ill-health from the Westminster Hospital. He had gained notoriety through keeping the embalmed body of his mistress in his bedroom, as a pioneer of ballooning, and as an explorer for whales. But he deserved recognition for his early work on the lymphatic system. Nurtured in the Hunterian tradition was John Haddy James. He was a native of Exeter, and with Samuel Barnes was a leader in the development of the Exeter school. He joined the staff of the Devon and Exeter Hospital after serving with Wellington at Waterloo, and two years later won the Jacksonian prize for an essay on inflammation. He invented many interesting mechanical devices and was noteworthy for having introduced continuous traction in the treatment of fractures. He was one of those who assisted Charles Hastings, of Worcester, in the foundation of the Provincial Medical and Surgical Association, which later became the British Medical Association. James became its president in 1842, and the next year was one of the original Fellows of the Royal College of Surgeons of England under its new charter.

Liverpool Medical Institution

Sir Henry Cohen read a paper on "The Collagen Diseases and their Response to Cortisone and A.C.T.H.," at a meeting on March 26. Reviewing their pathology, Sir Henry discussed the ways in which fibrinoid degeneration was related to collagen. Damage to the collagen system led to disturbance in the lubrication of tissue and the transport of metabolites. He then described four collagen diseases—diffuse lupus erythematosus, periarteritis acuta nodosa, temporal arteritis, and dermatomyositis—and pointed out that similarities of pathological findings did not necessarily imply similar aetiology. He thought that periarteritis nodosa and temporal arteritis were different entities. The discovery of A.C.T.H. and cortisone had helped in the unification of collagen diseases, since it was in them that their greatest effect was found. Great, however, as had been their benefits in these diseases, they were toxic drugs, of great theoretical interest, but which would soon be superseded by newer forms of therapy. After Sir Henry's paper the annual meeting of members was held. Sir Henry Cohen was elected president for the ensuing year and was installed by the retiring president, Mr. J. B. Oldham.

Manchester Medical Society

Discussing cancer of the breast at an ordinary meeting on March 24, Mr. Hedley Atkins said that at the Guy's Hospital Breast Clinic they were searching for criteria that would enable them to predict whether the response to hormone therapy was likely to be favourable or not. Although this foreknowledge was not essential in treatment with endocrine preparations, it would be almost indispensable if the operations of adrenalectomy and hypophysectomy were shown to have definite value. An investigation to compare the results of adrenalectomy and hypophysectomy was now proceeding.

North of England Otolaryngological Society

On March 20 Mr. J. M. Wishart was installed as president at a meeting held at the Blackburn and East Lancashire Royal Infirmary. Afterwards clinical cases were shown and discussed.

Correspondence

A New Oral Diuretic

SIR,—I had the opportunity of reviewing the January 16 issue of the *Journal* and was impressed with the annotation entitled "A New Oral Diuretic" (p. 144). I was intrigued by the statements made on behalf of the new diuretic "mercloran" ("neohydrin"), which in my experience has proved to be almost as good as the parenteral diuretics. In fact, maintaining patients oedema-free with mercloran has been consummated with less difficulty than with the more potent parenteral mercurials. Therefore I was somewhat puzzled by your rather high incidence of reactions. I could not imagine that severe gastro-intestinal symptoms "develop in about two-thirds of patients after effective doses," as you report.

In my experience[1] there have been fewer reactions with mercloran (about 10%) than with other diuretics. Moreover, the reactions when they occurred were usually mild. Considering the relationship between an effective diuretic dose and a dose large enough to provoke reaction, I have found that mercloran in nearly all instances will provide satisfactory diuresis in a dose far below the reaction level. This has been established in a report by Gold and his co-workers.[2] In addition to the high degree of tolerability which was observed in studies of over two years, I had also noted a psychological improvement in the patients. Apparently the lack of drastic response which the patients formerly experienced with the parenteral diuretic has improved the patient's attitude and nutritional status.

The Cornell University authorities, who have bioassayed this product and reported it to be unusually effective, had pointed out that in their tests the dose was necessarily administered *in toto*, even as high as nine tablets at once, and therefore some of the patients experienced gastro-intestinal reactions. The authorities also claimed that these reactions would certainly be less frequent if the doses were divided. This has been my experience and that of other investigators. It was more important to administer enough of the diuretic per day than per one dose. It is also well to point to the misconception clinicians have frequently entertained that mercurial diuretics give off metallic mercury. I believe that a review of the pharmacology texts will allay such fears. Organic mercurial diuretics do not give off free mercury. This also applies to mercloran.[3] According to this monograph,[3] in the test for purity on this agent, the results indicated absence of ionizable mercury and other heavy metals.

Kidney function tests are being done on all of the patients attending the cardiac clinic who have been taking mercloran for a duration of from one to two and a half years. At the present time, we have not found a single patient who has presented any clinical or laboratory evidence of impairment of kidney function due to the oral mercurial mercloran. This study will be published in the near future. Through my own experience and that of other investigators in the United States, we have gained full confidence in the oral mercurial diuretic such as mercloran. I believe the British clinicians will experience similar favourable and unequivocal results.—I am, etc.,

Newark, 8, New Jersey, U.S.A. WILLIAM A. LEFF.

REFERENCES

1 *J. med. Soc. N.J.*, 1953, **50**, 149.
2 *J. Amer. med. Ass.*, 1953, **152**, 1130.
3 Ibid., 1953, **152**, 331.

Congenital Tuberculosis after Pleural Effusion in the Mother

SIR,—The case described by Dr. Neil Mason (*Journal*, April 24, p. 970) is of great interest from the point of view of the pathogenesis of tuberculous infection generally, and of demonstrating a special need to distinguish primary from secondary tuberculous disease in pregnant women. The pleural effusion in the mother when five months pregnant was obviously a perifocal reaction associated with the benign primary complex. This condition does not benefit by chemotherapy as a general rule unless there are evident bacillaemic metastases (meningitis, bone and joint disease, etc.), but it may give rise in pregnant women, as in this case, to the fatal malignant primary complex in the foetus. As this condition in the foetus cannot be diagnosed until delivery, it follows that all pregnant women contracting the benign primary complex should have chemotherapy as a preventive of foetal tuberculosis.

In Dr. Mason's case the mother did not have chemotherapy during pregnancy, and she recovered clinically without it. The lesions found in the infant at death, eight days after full-term delivery, included a large caseous mass of lymphatic nodes in the area of the porta hepatis, and acute miliary foci of two distinct sizes in the lungs, spleen, and liver. These are the lesions of the malignant primary complex, complicated by acute miliary dissemination, and are invariably fatal without chemotherapy. The conditions in this case were entirely different from that of the pregnant women with any form of secondary tuberculosis, such as advanced fibro-caseous disease, where acquired resistance is strong throughout the course of pregnancy and constitutes an effective protection to the foetus, which in these circumstances is usually born healthy.

An interpretation of the sequence of events in Dr. Mason's case, based on the known facts relating to natural and acquired resistance in tuberculosis, is as follows. The mass of caseous lymphatic nodes could hardly be other than the lymphatic component of a malignant primary complex of which the primary focus in the stomach or duodenum was no longer to be seen macroscopically. The upper mesenteric site of these nodes strongly suggests infection of the foetus by the alimentary route, probably by swallowing infected amniotic fluid. Since the duration of the disease appeared to be approximately the same in mother and child, the amniotic fluid was probably infected at a very early stage in the pregnancy, and most likely during the incubation period of the infection in the mother. At this stage, a preclinical bacillaemia regularly occurs in tuberculosis, as in so many other infectious diseases, and this is usually brought to an end by acquired resistance which rises only after the primary complex is established. Infection by means of the amniotic fluid is usually massive in contrast with that by inhalation, and this would account for the large caseous mass of lymph nodes (malignant primary disease) with two later invasions of the foetal circulation giving rise to the two sizes of acute miliary foci in lungs, spleen, and liver.

A case like this is rarely observed and it should become classical. Its lesions are most important: (1) the danger to the foetus not only from malignant primary tuberculosis (acute miliary) but from benign primary tuberculosis in pregnancy; (2) the necessity to distinguish primary tuberculosis from secondary in general, and particularly because of the need for preventive chemotherapy for the foetus in the former; and (3) the neat demonstration of the operation of two fundamental factors in pathogenesis, quantity of bacilli, and acquired resistance.—I am, etc.,

London, N.W.8. M. SEKULICH.

Neomycin in Pyogenic Skin Diseases

SIR,—The reports by Dr. R. E. Church (*Journal*, February 6, p. 314) and by Dr. I. W. Caldwell (*Journal*, April 10, p. 871) suggest that neomycin may be the drug of first choice in the superficial pyodermas. But I would suggest that there may still be a place for other antibiotics. During the past 15 months, 304 cases of impetigo contagiosa all responded within a few days to treatment with 3% aureomycin cream. Of these cases 135 were sigilliform, and 169 were bullous and mostly widely generalized. It appears unlikely that insensitive organisms will develop in the course of rapid and successful treatment. Furthermore,

although it is generally agreed that neomycin may be applied topically with safety, it has been shown that systemic absorption may occur from topical application.[1] Although the serum concentration of neomycin was slight, this factor may have to be considered if local applications are adopted on a wide scale.

With regard to treatment of sycosis barbae, assessment is difficult but aureomycin and terramycin both appear to be of some value. Of 18 cases treated with 3% terramycin cream, 5 remained well when reviewed from 2 to 11 months after treatment had ceased, 4 cases cleared rapidly but did not report back, 3 cases continued to have occasional pustules, 1 case recurred 4 months after treatment had ceased, and 5 cases failed to improve. Six cases of seborrhoeic type showed temporary improvement. Of 28 cases treated with 3% aureomycin cream, 8 remained well when reviewed 2 to 18 months after treatment had ceased. Eight cases cleared rapidly but did not report back, 6 cases continued to have occasional pustules, 1 case recurred 11 months after treatment had ceased, and 5 cases failed to improve. Five cases of seborrhoeic type showed temporary improvement. As might be expected, duration of treatment was longer than in the cases of impetigo. In this connexion, the development of insensitive strains is of some moment also in treatment with neomycin, since neomycin may be required as an intestinal antiseptic and as a parenteral[2-6] antibiotic in selected cases. It has also been shown that, *in vitro*, increase in resistance develops more regularly and rapidly to neomycin than to aureomycin, terramycin, and chloramphenicol,[7] and that strains which have increased in resistance to neomycin also increase significantly in resistance to streptomycin.[7 8]—I am, etc.,

Glasgow, W.2. W. A. DEWAR.

REFERENCES

1 Livingood, C. S., *et al.* (1952). *J. Amer. med. Ass.*, **148**, 334.
2 Waisbren, B. A. (1951). *Arch. intern. Med.*, **88**, 467.
3 Kadison, E. R., *et al.* (1951). *J. Amer. med. Ass.*, **145**, 1307.
4 Nesbit, R. M., *et al.* (1952). *Antibiot. and Chemother.*, **2**, 447.
5 Knight, V., *et al.* (1952). *J. Amer. med. Ass.*, **149**, 1395.
6 Reed, C. E., and Wellman, E. A. (1953). Ibid., **152**, 702.
7 Gocke, T. M., and Finland, M. (1951). *J. Lab. clin. Med.*, **38**, 719.
8 Gezon, H. M., and Fasan, D. M. (1951). *Science*, **114**, 422.

Appointment with Fear

SIR,—Dr. P. R. Saville's timely letter (*Journal*, April 17, p. 932) entitled "Appointment with Fear" deplores the increase of unhealthy, and often unfounded, fears among the British public in recent years. In a clinical lecture, the late C. B. Lockwood stated: "The human being fears death above all things; after death he fears pain, and after pain, parting with his possessions."[1] Had he been speaking to-day he might have added the fear of official infringement of his rights and liberties.

There is little doubt that most people fear the idea of pain, although they will usually bear it stoically enough when they actually have to endure it. They also fear the loss of their possessions or the ability to earn their living, but I would dispute the categorical statement that they fear "death above all things." In health, most of us dislike the contemplation of our own demise, but when people are faced with its inevitability they generally do not seem to be afraid. It has been stated that even condemned prisoners become philosophical enough once they come to realize that their fate is inevitable. It is certainly the general experience that the mortally sick and the aged generally face the end with little apprehension and sometimes even with a sense of relief. This may also be the case with those who retain their full faculties throughout.

I believe that what most people dread is a sense of uncertainty and the unknown. They fear "the shadow of uncertain ill." When they know exactly what to expect they generally cease to be fearful. Even in such a dreaded disease as cancer, I have generally found that patients are quieter in their minds once their doubts have been resolved and when they have been frankly told the truth, particularly where some method of treatment can hold out a reasonable prospect of cure or amelioration. I have never found it advisable to attempt to delude patients into a sense of false security: they generally don't believe one if one does, and doubts as to the truthfulness of their medical adviser only tend to increase their general anxiety and augment their fears. On the other hand, no good purpose is served by proffering unasked-for information of an unpleasant character. A patient or his relatives should not generally be told bad news of this kind, unless the direct question is asked: exceptionally such information may become necessary in the patient's interests, particularly where there is hesitation to undergo some favourable line of treatment with a prospect of success.

We, as doctors, also have our especial fears, which have greatly increased in recent years: fear of the power of those authorities who now so largely control our professional lives; fear of irresponsible litigation, and, in view of some of the more recent decisions of the courts, a doubt that we may receive a full measure of justice; fear of the activities of other medical men who may be tempted to undermine our interests for their own advantage in the altered circumstances in which we now practise our profession. The most serious feature of these special medical fears is the unfavourable effect that they are having on the younger men and on entrants to the profession; this is evident from their increasing unwillingness to take appointments which carry any risk and their reluctance to undertake clinical responsibilities which should be well within their capabilities. Soon the most able types of men and women may cease to be willing to enter the profession at all. We may free our patients from unnecessary fears, to some extent, by clearing their minds of superstitions and by telling them the truth when we can, for ignorance is often the basis of fear; but neither we nor they can hope for freedom from fear unless we also regain some of those other freedoms which we seem to have lost. The public should remember that the doctor whose professional conduct is unduly influenced by the fear of personal consequences is lost, as may his patient be also.—I am, etc.,

London, W.1. JOHN NICHOLSON.

REFERENCE

1 *Clinical Lectures and Addresses on Surgery*, 1907, p. 4. London.

SIR,—The letter by Dr. Paul R. Saville (*Journal*, April 17, p. 932) sounds a welcome note of sanity. He has, however, omitted to point out that we should eat nothing but raw food to be entirely safe, for we have little, if any, notion of what happens to it during cooking. What thermal decomposition products, potentially lethal, has man been consuming for many thousands of years? We have no idea; nor have we a complete list of all the essential nutrients destroyed during cooking. Needless to say, this goes not only for cooking, but also for factory processing. How do we know, indeed, that many of the "thousand natural shocks that flesh is heir to" do not in fact come from producing slow poisons by simply cooking food or from the destruction in it of things we need?

Presumably the truly cautious should not eat anything cooked, processed, or manufactured before trying it on the dog—or at least on the laboratory rat. This, it seems, is the procedure being advocated in the field of food additives. Do we know what risks we run not just from preserving and sterilizing, but even from Mum's best kitchen practices? The answer is that we don't, any more than we know fully the hazards of crossing Piccadilly at midday; if we did, we should not get run over there, because we'd stay on our side.

There seems to be growing a pusillanimity that is a caricature of "safety first" in food, and the nation is, I submit, at present in serious danger of suffering from acute hypertoxiconsciousness—to coin a word. Scientists, whether medical or non-medical, surely have a responsibility for preventing the spread of this condition. Unfortunately, many of them seem to be doing exactly the opposite.—I am, etc.,

London, N.W.3 A. L. BACHARACH.

Smoking and Lung Cancer

SIR,—The considerable suggestive evidence of a positive relationship between lung cancer, heavy cigarette-smoking, and urban residence may mean that (leaving out of account the possibility that city people smoke more than countrymen) excessive cigarette-smoking develops some abnormal mechanism which allows the ingestion not merely of possible carcinogens from the cigarettes themselves but, in addition, known potential carcinogens polluting the surrounding atmosphere. In short, two seemingly highly important factors—cigarette-smoking and urban residence—may operate synergetically. Heavy cigarette-smoking appears sufficiently to irritate the mucosa of the respiratory tract to cause catarrh, bronchial wheezing, and reflex coughing, which continue for as long as the smoking habit persists. In industrial areas particularly, the discharge is impregnated with dark particles, including atmospheric soot. Pipe-smokers who do not inhale deeply through either mouth or nostrils appear generally to avoid this irritation and discharge.

The present writer found that a chronic "smoker's cough" which developed after heavy smoking (20 to 40 cigarettes per day) ceased immediately he gave up cigarettes. It did not reappear after pipe-smoking. Yet a mere ten cigarettes per day, even without deep inhalation through the mouth, was enough to start it off again together with a characteristic bronchial wheezing and discharge. It was believed that voluntary and involuntary inhalation of cigarette-tobacco fumes through the nostrils into the nasopharynx and bronchi might be the cause. When a cigarette-holder (with or without filter) was used, the cigarette end, as with the bowl of a pipe, was projected far enough from the nostrils to avoid nasal inhalation. Thereafter an abnormal experimental number of cigarettes (50 to 60 per day) was smoked for a week without the reappearance of the former symptoms.

It is probable, therefore, that nasally inhaled tobacco smoke caused nasopharyngeal and perhaps bronchial irritation, hypersensitivity of the mucosa, and a relatively copious watery discharge from neighbouring glands. It is not impossible that if a sufficient flow of fluid was generated by nasopharyngitis and bronchitis, this would cascade over the cilia of the respiratory trees, defeat their cleansing mechanism, and thus allow the carriage of tobacco soot and, in addition, inspired atmospheric soot into the bronchioles and alveoli. There is already experimental evidence[1 2] that radio-opaque dusts mixed with fluids and introduced into the trachea of cats did penetrate right into the alveoli. The cilia were rendered inoperative by the fluid.

Although it is more reasonable to assume that a nasopharyngeal secretion would be blocked at the epiglottis and pass down the oesophagus, the wheezing and bubbling in the bronchi of habitual cigarette-smokers suggest that fluid (unless it is all produced by a local bronchitis) may indeed creep into the bronchi at night without operating a cough reflex. The matter was attacked experimentally by the introduction into the nasopharynx of "dionosil" in successive evening dosages of 6, 10, and 12 minims (0.3, 0.6, and 0.7 ml.) respectively after heavy cigarette-smoking without holder. Radiography showed a negative result—the material apparently went down the oesophagus, although rales and rhonchi could be detected with the stethoscope each morning. It is possible that the oily suspension used was insufficiently dilute to pass over the epiglottal bridge. A second attempt, involving the like ingestion of radioactive gold colloid, was projected, but this has not been made since there appears to be already available clinical evidence that a post-nasal drip does sometimes overcome the cough reflex and result in a mucous creep into the bronchi. Among children in particular lipid pneumonia can occur in healthy individuals after "the prolonged use of an oil spray or the instillation of oil in the upper respiratory passages."[3]

Even if the irritation induced by inhaled smoke is confined to the bronchi, the working hypothesis that inspired particles of atmospheric soot, as well as those of burnt tobacco, may be caught up in a mucus discharge and carried deep into the lungs is not invalidated. It matters little whether the abnormal flow of mucus is produced in the nasopharynx or in the bronchi so long as it is sufficiently copious to entrap inspired foreign particles, to overflow the cilia in such a way as to carry injurious substances into the bronchial terminations, and to prevent the cilia from expelling them.

The present contribution is made in the hope that the problem raised will be attacked experimentally by others directly interested in cancer research. It should be possible to achieve hypersensitivity and a chronic respiratory tract discharge in a series of experimental animals and to introduce, over a period, concentrates of tobacco soot, atmospheric soot, and mixtures of both. The writer of course makes no claim to the validity of the present hypothesis, but at the same time he now proposes to use a pipe, or a cigarette-holder at least three inches long, to avoid unnecessary future irritation of his respiratory tract epithelium.—I am, etc.,

A. J. MARSHALL.

London, E.C.1.

REFERENCES

1 Barclay, A. E., *et al.* (1938). *Brit. J. Radiol.*, **11**, 405.
2 —— (1940). Ibid., **13**, 410.
3 Holt, L. E., and MacIntosh, R. (1953). *Pediatrics*, 12th ed. New York.

Skin Cancer and Burns

SIR,—It is desired to correct a statement in your annotation "Skin Cancer and Burns" (*Journal*, January 23, p. 204). The paragraph, which could be misinterpreted, reads: "Cancer of the skin, after years of actinic rays, is common in such countries as Australia, where it is found that European settlers are most susceptible."

In our statistical survey[1] of patients with cancer of the skin, the following facts emerged: (1) The average age of patients with cancer of the skin, born in Australia, is 61. (2) The average age of patients with cancer of the skin who have migrated to Australia (of these 99% come from Great Britain and other European countries) is 71. (3) The average length of residence in Australia (of the non native-born) before the development of skin cancer is 44 years.

In our opinion, the development of skin cancer is far more common among people of British descent than people of any other race, including the Scandinavian and North German.—I am, etc.,

W. H. WARD.
W. W. GUNTHER.

Newcastle, Australia.

REFERENCE

1 Ward, W. H. (1952). *Aust. J. Derm.*, **1**, 157.

Cancer Resistance

SIR,—The article on neuropathies associated with carcinoma by Dr. P. L. de V. Hart (*Journal*, March 13, p. 606) makes fascinating reading. I have under investigation at present a patient with foot drop and radiological evidence of bronchial obstruction, who "feels well" yet nevertheless may be doomed; but it raises wider and perhaps fundamental issues of practical importance. The far-flung effects of cancer are not always due to metastases. Multiple venous thromboses in areas remote from the growth may appear and disappear after a short interval (Trousseau's syndrome). I have seen small, slightly tender thromboses in the elbow appear and pass in a week or so, followed by similar episodes in the leg and chest (transitory pleurisy), heralding the major symptoms of a carcinoma of the tail of the pancreas. The rare myoclonus of the palate is said to be a pointer to lung neoplasm, without actual bulb involvement. There is undoubtedly a biochemical factor in these cases, perhaps some change in the serum producing remote effects. Now all experienced practitioners have met the occasional case of carcinoma that surprisingly seems to come to terms with the neoplasm and lasts many years,

I recall a lady who had a carcinoma of the caecum removed, to be followed 12 years later by a carcinoma in the colon, also excised (both dealt with by the late Mr. B. J. Ward). She developed a large irregular liver years later and was alive over 26 years after the first operation, despite the hepatic enlargement. Of course, long-standing cases of breast carcinoma are much commoner, and are usually explained by "fibrosis," but I am by no means certain that either the scalpel or the scirrhus explains away these cases. In my view there is a resisting factor in the serum in certain favoured individuals, and I am sure there are sufficient cases up and down the country to warrant an investigation of the serum of these carcinoma-resistant people.

I wrote to the *B.M.J.* some years ago on this matter, but it raised no interest. The high incidence of certain types of carcinoma in the same family (I have seen uterine cancer in a mother, later followed by the same type of neoplasm in three daughters, all the latter in the early 40's), suggests that there might even be an association between particular types of carcinoma and blood groups (the latter, of course, in the widest sense).

The effects of the endocrines in the treatment of some forms of malignancy suggest that the body could produce some defensive response, albeit too weak to be effective unless considerably enhanced artificially, in parallel fashion to cortisone. The answer to smallpox and scurvy was found long before virus and ascorbic acid deficiency were associated as causal, and the answer to neoplastic disease could possibly be found on these lines long before the scientists give us chapter and verse.—I am, etc.,

London, S.W.2. A. WISEMAN.

Cortisone and Infection

SIR,—Your leading article entitled "Cortisone in Infection" (*Journal*, February 13, p. 381) is of very real interest. I shall be most obliged, however, if you will publish this letter as, in a sense, rebuttal of one sentence—namely: "It seems that, whenever cortisone has been administered to a vertebrate host parasitized by an invertebrate, the course of events has been altered to the detriment of the host."

There is no question that administration of large amounts of corticoids (A.C.T.H., cortisone, or hydrocortisone) to patients or to experimental animals with a variety of infections will tend to cause a dissemination of such infection usually to the detriment of the host, unless suitable means are employed to counteract such detrimental effects. There is, however, a very real place for the use of these hormones in the clinical management of infectious disease. This use is limited, for the most part, to infections for which thoroughly adequate antibiotic agents are available. Specific indications for the addition of intensive hormonal therapy to appropriate antibiotics consist in an overwhelmingly severe infection, with particular reference to generalized peritonitis, unusually virulent forms of pyogenic meningitis, with or without obvious blood-stream infection. If one employs A.C.T.H. and cortisone in a suitable manner in such individuals, using the hormones for their "non-specific antitoxic and anti-shock effects" to tide the individual over until the antibiotics have a chance to take effect, significant improvement in mortality and morbidity will result. Such therapy was undertaken on an investigative basis almost four years ago in this institution, and has now become routine in infections of more than usual severity.

Incidentally, it is our feeling that there are very few of the untoward effects of the corticoids, in so far as infection in the human subject is concerned, which cannot be reasonably well explained on the basis of inhibition of the inflammatory reaction. On the other hand, such inhibition can be highly desirable in the case of inflammatory involvement of the central nervous system, assuming that one has available an antibiotic capable of destroying the organism. A paper giving a comprehensive review of our total experience to date appears in the current volume of the *Journal of Pediatrics*.—I am, etc.,

Oakland, 6, California LAURANCE W. KINSELL.

Elderly Psychiatric Patients

SIR,—Why do psychiatrists (and psychologists) habitually misuse their own special language? In the *Journal* of April 10 (p. 876) there is a letter in which a psychiatrist discusses the case of "elderly psychiatric patients" (though you, Sir, or the Assistant Editor, are, I fear, responsible for the actual headline). What is an "elderly psychiatric patient"? The answer *should* be "an elderly patient practising psychiatry"—so odd a combination that, of course, we reject it as the writer's meaning.

One is constantly reading of "psychiatric disorders," "psychiatric disability," "psychiatric symptoms"; but the writers do not *mean* disorders affecting the treatment by a psychiatrist, or affecting the psychiatrist himself—or a disability affecting the psychiatrist or affecting his treatment—or symptoms affecting the psychiatrist. No, what the writer means by "elderly psychiatric patients" is "elderly patients with mental disease under treatment by a psychiatrist." The term "psychiatric" is transferred from its proper subject, the psychiatrist, to his patient. But if psychiatrists habitually misuse their own language one begins to question the soundness of their reasoning.

I do not venture to suppose that this protest will avail anything. The misuse of the word "psychiatric" constantly recurs even in textbooks on psychological medicine by authors of acknowledged authority. Medicine is full of terms habitually, though wrongfully, misused. To name only a few there are "the acute abdomen," "the acute ear," T.B. (for "tuberculous" or "tuberculosis"), etc., etc. Very many years ago the Editor of the *B.M.J.* published a short leading article on the last of these abuses above-mentioned following a letter from me pointing out that it was sometimes impossible to say whether "No T.B. found" in a report on a demobilized soldier (after War I) meant "No tubercle bacilli found" (on sputum examination), or "No tuberculosis found"—a difference of vital importance. Did the kindly intervention of the Editor result in any change for the better? No. "T.B." stands triumphant. I have, in the past, even been referred to—through ministerial channels—as "T.B. officer." What chance for "psychiatric"? Still, let the protest stand; it can, at least, do no harm.—I am, etc.,

Folkestone. E. WEATHERHEAD.

Psychiatry and General Medicine

SIR,—Having read the excellent article by Sir David Henderson (*Journal*, April 17, p. 889) I feel sure that he will be the first to admit that much of the disrepute enjoyed by the psychiatrists is of their own manufacture. The acceptance of a form of therapy by the medical profession as a whole depends ultimately on the response of patients to treatment. It has always surprised me that psychiatrists never seem to discuss treatment. As a rule they can always find a cause for a symptom or a syndrome which satisfies them, even if no one else, but, in most cases, that is as far as it goes. They wish to be accepted by all as openly as general physicians and surgeons, yet their form of treatment is nebulous and shrouded in mystery. Even standard textbooks devote little space to the management of cases except for those ill-understood forms of therapy, such as insulin, which even Sir David Henderson states are too readily used.

I would willingly send more of my patients with anxiety neurosis (and all doctors see large numbers of them) to the psychiatrist were he more helpful to me. We certainly need help with these cases, but little real improvement seems forthcoming. We get numerous labels for their inadequacies and weird causal agents for their symptoms, but their future seems quite unpredictable, except in so far as it will be the same as their past. The psychoses seem to be largely incurable, though some change may take place as a result of an empirical form of therapy or destructive brain operation. Any improvement seems usually to be short-lived. The psychoneuroses seem even less amenable

to psychiatric treatment, and it is with this group in particular that I plead for more constructive help from the psychiatrists. There is certainly enough material for them to treat.

I have stated elsewhere[1] that in my opinion the child psychiatrist is not always as helpful as the paediatrician. As an example, one may take the favourite topic of enuresis. My own view, being that of a person who likes a convenient "organic" basis for disease, is that it is usually due to a disordered sleep mechanism in which control by the higher centres is so completely lost during too deep a sleep that reflex emptying of the bladder occurs. Fundamentally, the process is similar to that occurring in incontinence in organic disease, for example paraplegia. Treatment of childhood enuresis with the amphetamine group of drugs produces remarkable results—far better than does the delving of the psychiatrist who searches for emotional factors. He does not seek such factors in the bed-wetting of paraplegics. Whilst doctors are investigating the fascinating field of psychosomatic medicine, it is becoming more evident that many so-called functional diseases have an organic basis. It may well be that the psychiatrist will be called on to become more of a physician than the converse.

Finally, to Sir David Henderson, I would tell him of the most recent instance when I asked the help of a psychiatrist. It was concerning an obsessional neurosis, and the patient would 'phone me repeatedly during the night to explain his fears. After being examined carefully by the psychiatrist and the cause of his symptoms being discovered, came the question of treatment. I was advised that the only solution would be to remove the patient from my list and let him plague the life of some other unfortunate doctor. Is it surprising that we are not yet all endeared to the science of psychiatry?—I am, etc.,

London, S.E.24. CYRIL JOSEPHS.

REFERENCE

[1] *British Medical Journal*, 1952, 2, 881.

SIR,—As one who has come into the field of psychotherapy from a fairly broad background of hospital medicine and general practice, I would like to make a few comments on Sir David Henderson's address (*Journal*, April 17, p. 889). Much of my work is at a clinic for the out-patient treatment of neurotic disorders, where analytical psychotherapy is used, and where lay therapists are employed under supervision by the medical staff. Even though there are other out-patient clinics staffed by doctors, between 700 and 800 new patients are referred to us each year, mainly by general practitioners. Over a number of years I have not come across a case of a patient refusing treatment from a lay therapist, or complaining at being allotted to one. Nor have there been any instances where a lay therapist's lack of medical knowledge has been a stumbling block to satisfactory treatment.

As a healer, the lay therapist seems to possess several advantages over many doctors in the treatment of the neuroses. His professional status does not act as a screen between himself and his patient. His understanding of the patient is not limited by the narrow, mechanistic training of the medical curriculum, with its emphasis on factual and textual knowledge. His vision of the whole person is not obscured by anxiety concerning any disease that the patient may have. His treatment does not tend to be applied *secundem artem* after a diagnosis, but rather according to his understanding of the patient's needs. He has no professional overhead expenses, and therefore the amount of time he can give to each patient is not limited primarily by economic considerations. In general, patients referred to clinics would seem to require treatment over a period of a few or a great many months with an average of two sessions per week; and it is difficult to see how, under the conditions of general practice to-day, a doctor can give adequate treatment to his neurotic patients. Undoubtedly many physicians help and support their patients in their difficulties, but that is not the same as curing them and rendering them independent of their doctor's help.

In regard to the proper training of medical students "to deal intelligently and skilfully with patients as persons," I wonder whether lectures and scientific knowledge are the best means of achieving these aims. There is a danger in the over-development of the intellectual function, so that the natural intuitive understanding becomes stultified. Probably one of the most important things of all is to be able to listen to patients—to the unspoken as well as the spoken word, and to the unconscious. The Chinese emphasize this in their proverb, "If you want good advice, go to a man with four ears." Many of our patients who have been under psychiatric care have had no opportunity to be listened to, and this often is their greatest need.

Surely the needs of our patients should be our primary consideration, and until the supply of physicians is sufficient to meet their needs, both in mental hospitals and in out-patient clinics, many patients will fail to get the help they require unless the lay therapists are valued for what they can do.—I am, etc.,

Edinburgh, 4. PHILIP SCOTT.

Second Attack of Chicken-pox

SIR,—We were interested to read the extract from Dr. J. I. Lyons's letter (*Journal*, April 10, p. 878). We have in fact seen only two instances of second attacks of chicken-pox this year, but the history of one is, we feel, worthy of note.

The patient is a healthy girl, now aged 8, who developed chicken-pox on June 23, 1953. This ran a normal course and she quickly recovered. On January 27, 1954, one of us again saw her with a mild but again quite typical chicken-pox rash, ushered in by a mild systemic upset and a temperature of 99° F. (37.2° C.). Again she recovered quickly. We were therefore amazed and indeed not a little suspicious when in April 1 we were asked to see M., who "had another rash." Sure enough she had chicken-pox. On each occasion the rash has been preceded by a mild systemic disturbance; the elements of the rash are typical, the centripetal distribution, the intraoral vesicles, and the "cropping" have been present on each occasion, and indeed in the third attack she even showed a concentration of vesicles at the site of a recent abrasion on the left elbow.

We are at a loss to explain these three attacks in so short a space of time and can only postulate different strains of the virus, immunologically distinct, or alternatively a complete failure to develop immunity to the virus. This latter theory would explain individual cases, but would not account for Dr. Lyons's observation of second attacks.—We are, etc.,

JOHN C. TURNER.
SIDNEY ABRAHAMS.

London, E.11.

Herpes Zoster and Chicken-pox

SIR,—That there is a very close association between the viruses of herpes zoster and chicken-pox is well known, but the following case is, I think, something of a rarity and therefore merits recording.

On April 10 a woman aged 58 consulted me for an eruption which had appeared on the previous day. This was situated on the right hip, the right flank, and the upper and outer part of the right thigh, and consisted of typical papulo-vesicles of herpes zoster. She had had no pre-eruption pain and the rash was not troubling her much at the time, and so I prescribed a placebo mixture and an occlusive varnish. On April 15 I received a message asking me to call and see her as she was not so well. She told me that she had had little sleep during the previous two nights owing to pain having developed in the eruption. She also said that she had developed more of the eruption in various places. When I asked to be shown these fresh lesions she exhibited to me scattered papules and vesicles on the face, trunk, and limbs, more or less symmetrically arranged, and which were indistinguishable from the lesions of chicken-pox—there was no grouping about these fresh lesions such as was present in the earlier zoster eruption—and I have no doubt whatever that this patient had developed an outbreak of true chicken-pox within a week of the appearance of her zoster eruption.

I have not heard or read of a similar case and I certainly have never seen one like this previously, and I should be most interested to learn if any other of your readers has had any experience of this double eruption, which appears to me to be strong evidence in favour of the viruses of zoster and chicken-pox being identical.—I am, etc.,

Birmingham, 18. C. SPENCER WHITEHOUSE.

Appendix in Hernial Sac

SIR,—I am not a little surprised to see from recent case reports in the *Journal* how uncommon it is to find an appendix in a hernial sac. I remember having removed two appendices whilst I was a senior registrar in the Royal Liverpool United Hospital. However, I observe that no one has reported an appendix in a left inguinal hernial sac. The patient, a Fijian aged 30, was admitted to Lautoka Hospital on September 21, 1953. He had developed acute pain in the left inguinal hernia, which he had had for three years. He was shocked, and he had a swelling in the left side of his scrotum "the size of a mature coconut." As soon as possible I operated and found in the left sac strangulated caecum, appendix, and 15 cm. of small bowel. He also had a hydrocele. Owing to the tenseness of the caecum it was not possible to exteriorize both ends of gut in the hernial sac and await recovery for a second operation: the gut was punctured by inserting a catheter fastened with a purse-string suture. After this collapse had been effected the neck of the sac was dilated and the whole mass was handed through to another incision in the right iliac fossa and exteriorized. After removal of the testis and hydrocele the hernia was closed with drainage. The gangrenous bowel was removed and the peritoneum was also drained. As might be expected, the patient died, but not until the fourth post-operative day.—I am, etc.,

Suva, Fiji. ROBERT I. COHEN.

Fatal Bronchial Asthma

SIR,—The article by Drs. C. Kelman Robertson and Kenneth Sinclair (*Journal*, January 23, p. 187) interested me considerably, as, in 26 years in practice, I have seen only three deaths from asthmatic attacks, and they all occurred in the year 1947.

Without records available, I can only write from memory. Case 1 was a man of 50, Case 2 a man of 35 approximately. Both these men had had repeated injections of adrenaline over more than 24 hours without much relief, and were given morphine. What part the latter played in the deaths is uncertain, but I have never used it in this complaint since. Case 3 was a young woman, aged 17, slightly built, very intelligent, working as a newspaper reporter, who had had asthma since infancy. She had been in good health and free from asthma for several months. About 15 minutes after a normal meal she developed an attack of asthma, presumably no worse than her usual ones. When the attack had been in progress for half an hour she suddenly collapsed. I was sent for and arrived within five minutes to find her pallid, pulseless, and with only an occasional sighing respiration. Intracardiac adrenaline had no effect, and she was dead within five minutes more.

My impression at the time was that she died of right heart failure, brought on by the strain of the attack. The views of Drs. Robertson and Sinclair on the possible mode of death in this case would be appreciated.—I am, etc.,

Wellington, N.Z. A. RYDER-LEWIS.

Clinical Aspects of Bronchial Obstruction

SIR,—On reading the article by Dr. Robert N. Johnston *et al.* (*Journal*, April 3, p. 799) I was reminded of a sign of bronchial obstruction which I have recently observed and which is not mentioned by these authors, probably because it is rare or even unrecognized. It is a sign of partial obstruction in the sense that while it is complete in full expiration the dilating bronchus during inspiration allows air to pass *at a certain stage*. On auscultation before this stage air entry is absent, but when it is reached there is an accelerated rush of air past the obstruction due to the increased negative pressure built up beyond it, so that a rather sudden, loud, but short, soufflé results towards the end of the inspiratory phase.

I have heard and demonstrated to my registrar this unmistakable finding in two children, in each case over a lower lobe; the mechanism was demonstrated by bronchoscopy showing polypoid tuberculous granulations completely obstructing the bronchus in expiration, but incompletely in full inspiration. As mobility of the bronchus is so important in the production of this finding, it is evidently much less likely to occur when the obstruction is due to a carcinoma. I provisionally labelled the sign "delayed inspiration" and wondered what relation it might bear to the "veiled puff" described by Skoda in bronchiectasis. While such cases could well give a similar finding with a plug of sputum as the obstructing agent, forced coughing should easily differentiate this group by causing disappearance of the sign.—I am, etc.,

Bristol. J. E. G. PEARSON.

Diabetes Insipidus Associated with Pulmonary Disease

SIR,—I was very interested in Dr. J. E. G. Pearson's description (*Journal*, March 20, p. 704) of the diagnostic use of the serum tuberculin-neutralizing factor in sarcoidosis. However, I note that in order to carry out the test he injected his patient's serum into five other (tuberculin-positive) patients. May I most strongly urge him, or anyone else intending to carry out the test in the future, to keep for the purpose a small stock of guinea-pigs rendered tuberculin-positive with B.C.G.? It seems to me unwise to submit other patients to the risk of the transmission by means of a test of this kind of the virus of "serum hepatitis"—or even of a hypothetical sarcoidosis-causing agent.—I am, etc.,

London, S.W.1. G. R. F. HILSON.

Photic Convulsions

SIR,—I was interested in your annotation on "Photic Convulsions" (*Journal*, April 17, p. 925). I have found from a clinical point of view that glare and also the flicker from cinema screens will precipitate migraine in a number of cases, and I am hoping to be able to get more controlled evidence on this point in the near future. A main source of trouble is fluorescent tube lighting when the tube is parallel to the desk instead of at right-angles to it. It happens occasionally that glare is the predominant factor among other precipitating factors in a given case of migraine, and all that is required is to deal with this by the use of "polaroid" glasses, etc. It would appear that there are many industrial processes where the lighting conditions are such as to be excessive and to constitute a state of glare.

Certainly the visual experiences described by Dr. Grey Walter in *The Living Brain*[1] using flicker in phase with the alpha rhythms would seem to be similar to the scintillating scotomata of migraine. One of my patients, an industrial research physicist, volunteered the information to me that headaches were induced by the flicker of light through the trees by the wayside while motoring; which has features in common with a case mentioned by Dr. Grey Walter in the same book. The effect of glare and light on various forms of psychosomatic disease has been noticed in days gone by, and Liveing, in his book on "megrim,"[2] discusses it as a precipitating factor in asthma as well as migraine.—I am, etc.,

Birmingham, 27. K. M. HAY.

REFERENCES

[1] *The Living Brain*, 1953. London.
[2] *On Megrim*, 1873. J. and A. Churchill, London.

Weight-lifting

SIR,—I have a practice within a few hundred yards of London and Katherine docks, and see many stevedores suffering from "sprung back" or prolapsed disk. Questioning those injured in lifting suggests: (*a*) Breathing is an important factor. If the lifter exhales during effort this decreases intra-abdominal tension and relaxes any "antagonist" muscles. This tip is well known to professional weight-lifters. (*b*) The centre of gravity must be as near

to and as far below the object to be raised as is possible. (*c*) If two people are lifting they must act as "mirror" images. The Safety Health and Welfare Museum in Horseferry Road, London, S.W.1, shows the posters Dr. J. H. Cyriax mentions (*Journal*, April 17, p. 933), and also some models.

Packing-case manufacturers could do some research into the placing and use of inset metal handles in their products of standard-size soft wood.—I am, etc.,

London, E.1. N. D. WAYNE.

SIR,—"Your recent correspondence under the heading, "Advice on Weight-lifting" (*Journal*, March 20, p. 703, and April 17, p. 933) prompts me to mention that, in collaboration with the Central Council for Physical Recreation, this Society has for two years been running courses in manual lifting and handling all over the country. The original point of contact—and this is typical of our work—was that the knowledge and experience behind the training of the weight-lifter in the field of sport might well be applied to weight-lifting at work. From this purely speculative idea developed a joint interest in human kinetics, the physiological details being medically approved. The basic lessons taught in these courses are summarized in a fully illustrated pocket book, *Manual Lifting and Handling*, which is bought by industrial firms in sufficient numbers to justify the belief, which we share with your correspondents, that the preventive approach is both necessary and appreciated. —I am, etc.,

London, W.1. THOMAS FASSAM,
Controller,
Programmes and Publications,
Industrial Welfare Society.

Conjoined Twins

SIR,—I read with great pleasure Professor Ian Aird's account of the conjoined twins of Kano (*Journal*, April 10, p. 831), and I was interested in his statement that it has never been completely proved that conjoined twins are, in fact, invariably monovular. If conjoined twins were, on occasion, the result of fusion of binovular embryos would we not sometimes find that the twins were of opposite sexes? There is no mention of any such case in Professor Aird's paper, and I would be interested to know if conjoined twins of different sexes have ever been reported. It may, of course, be that the circulatory connexion between the two partners, with the resultant mixing of sex hormones, would render the development of normal sexual characteristics impossible, and some bizarre effects might result.

I understand from a veterinary colleague that authentic cases have been recorded of conjoined twins in other mammals where the partners are male and female, but I am afraid I can trace no written authority for this statement. —I am, etc.,

London, W.C.1 D. A. BAILEY.

Weber–Christian Disease

SIR,—The point of interest to me in Dr. H. R. F. Macdonald's medical memorandum on Weber–Christian disease (*Journal*, February 13, p. 377) was the admission of the patient to hospital as a case of coronary artery thrombosis. No evidence of myocardial infarction was found. Similar cardiac symptoms developed in a patient whom I saw recently with the same condition.

An obese woman aged 54 developed the typical lesions on her legs on January 10, 1954. She was seen by Dr. Alice Carleton on January 20, to whom I am indebted for the diagnosis. She was admitted to hospital for investigation and biopsy of one of the skin lesions, which confirmed the diagnosis. She showed a low grade pyrexia. This is her first attack, so that her condition cannot truly be termed "relapsing" nodular panniculitis. The skin lesions had resolved, when, on February 8, she suddenly "collapsed" and became breathless and cyanosed. She denied any pain. On examination auricular fibrillation with a ventricular rate of 150 per minute was found to be the cause of her symptoms. The blood pressure was 180/110. Treatment with digitalis was given, and the ventricular rate was reduced to 90 per minute. Sinus rhythm had returned when she was seen on February 15, and this has been maintained. An electrocardiogram could not be taken during the acute phase, but the tracing on March 12 was normal. A chest *x*-ray showed moderate generalized cardiac enlargement with unduly prominent pulmonary vascular shadows.

Lesions of the internal adipose tissue have been reported,[1] and it has been suggested that nodular panniculitis in the bone marrow can disturb normal haemopoiesis. Is it possible that similar lesions in the epicardial and pericardial fat may cause cardiac irregularities?—I am, etc.,

Wroughton, Wilts. W. L. CALNAN.

REFERENCE

[1] Steinberg, B. (1953). *Amer. J. Path.*, 29, 1059.

Treatment of Threadworm Infestation

SIR,—When faced with cases of threadworm infestation many of us seem to be preoccupied with giving medicinal vermicides, necessary though they may be, and ignore the underlying causes. The literature is confused on the subject, and I would welcome the views of other practitioners on the following questions.

What are the conditions which favour the hatching of threadworms in the bowel? Donald Paterson[1] says: "It is the opinion of the author that most people are constantly ingesting the ova of worms. Those who are below par and run down have a low hydrochloric acid content and therefore fail to digest and kill off the swallowed ova." Has any work been done to prove or disprove this theory, or to establish what are the conditions in the digestive tract which favour the hatching and growth of the worms? Unless the problem is tackled at this level the tendency to infestation cannot be cured, however efficient the vermicide may be for each attack.

Is threadworm infestation detrimental apart from the anal irritation and the very rare blocking of the appendix? My own experience among well-cared-for children leads me to think that the appearance of threadworms is the result of debility rather than the cause of it. But what do others think? If, indeed, the condition is not detrimental there is no point in making the treatment more troublesome than the worms. Such fearsome and bothersome procedures are sometimes prescribed that mothers naturally get the impression that threadworms must be very dangerous, and become almost neurotic in their frantic efforts to eradicate the pests. I have recently heard of a mother who, when one of her family is infested, nightly gives enemas to her five children, including a baby, with goodness knows what psychological effects. She doses them and purges them and starves them, she daily boils their bed-linen and pants, and I am sure she would boil the children too if she could, so frantic and determined are her efforts to eradicate what she has been led to consider as a disgraceful and dangerous infestation. The tragic thing is that these efforts are largely in vain, because the worms appear again a few weeks later.—I am, etc.,

Shoreham-by Sea. GWYNETH M. COTTERELL.

REFERENCE

[1] *Sick Children*, 1938, p. 517. London.

Cricket

SIR,—A match between the B.M.A. and the Law Society Cricket Club has been arranged for Sunday, May 30, at 11.30 a.m., at Hurlingham, London, and I have been asked by Council to make the necessary arrangements on behalf of the B.M.A. Would any members who are active cricketers and who might wish to play please get in touch with me as soon as possible, so that an appropriate side may be chosen to represent the Association? Would members when writing please indicate their "potentialities"? Last year we were without a slow left-hand bowler, an omission which should be remedied this year.—I am, etc.,

The Little House,
Broadwater Down,
Tunbridge Wells. R. PROSPER LISTON.

Obituary

Dr. H. U. GOULD died very suddenly on April 14 in the grounds of his home at Walton-on-Thames, where he had been living in retirement, at the age of 78. Harold Utterton Gould was born at Worcester Park, Surrey, on February 18, 1876, the son of Charles Gould, Q.C., and was educated at Winchester, Trinity College, Cambridge, and St. Bartholomew's Hospital. He qualified in 1902 and graduated M.B., B.Chir. in the following year. After holding the appointment of assistant house-surgeon at the Gloucestershire Royal Infirmary and Eye Institution, he returned to St. Bartholomew's as resident midwifery assistant and house-physician. In 1906 he settled in practice at Shaftesbury, in Dorset, where he became medical officer to the Westminster Memorial Cottage Hospital and medical officer of health to the Shaftesbury Rural District Council. He took a prominent part in local affairs and was elected mayor of Shaftesbury. Dr. Gould returned to Surrey in 1926, living first at Surbiton and then in the adjoining Royal Borough of Kingston-upon-Thames, where he designed and had built a central surgery for the use of himself and his two partners. For many years a member of the honorary medical staff of the Kingston Victoria Hospital, he was much concerned about the closing of the hospital three years ago. He was also on the honorary staff of the Surbiton Hospital. A tall man, with the physique of an athlete—he rowed for the Leander Club and won the Colquhoun sculls while at Cambridge—he was remarkably gentle in treating his patients, who quickly found that his seemingly off-hand manner masked a keen interest in their welfare. Dr. Gould retired from practice two years ago, but made many return visits to the Kingston district to call on former patients who had become his friends. A widower, he is survived by two sons and a daughter.

Dr. MABEL G. BRODIE died suddenly on April 21 at Port Dickson, Malaya, at the age of 64. Mabel Garland Cowper was born on May 28, 1889, and was educated at the Universities of Aberdeen and St. Andrews, graduating M.B., Ch.B. from St. Andrews in 1914. After graduation she was resident for a short time in 1914 at the Birmingham General Dispensary, whence she went to the Brownlow Hill Infirmary, under the Select Vestry, at Liverpool. In this post she proved herself an able clinician, but her chief interests were in maternity and child welfare and in ophthalmology. She took the D.P.H. at Liverpool in 1917. After about two years she was appointed to one of the Liverpool fever hospitals, where her work and ability attracted the attention of the then medical officer of health, the late Dr. E. W. Hope, and he asked that she be appointed as first medical officer in charge of maternity and child welfare work for the city of Liverpool. Her broad view of the duties of such a post, along with her advanced outlook and ability, soon showed how far-sighted had been the choice of the Liverpool City Council. Her next appointment was to the staff of the Ministry of Health, but on her marriage to Dr. William Hugh Brodie she resigned from the Ministry. Shortly afterwards she became senior medical officer to the maternity and child welfare department of the Durham County Council. Later both she and her husband joined the Colonial Medical Service in Malaya. In 1933 she took the D.T.M.&H. of the English Royal Colleges. Dr. Mabel Brodie had very deeply at heart the interests of mothers and children, both in England and Malaya. She returned to England soon after the outbreak of the last war and was employed as a medical officer in an ordnance factory in Yorkshire, and later undertook public health work in Willesden and Islington. After the war she went back to Malaya, and her sudden death has deprived the Colonial Medical Service of a very capable and conscientious practitioner and administrator. She was a most generous and sympathetic person and will be missed by many of her colleagues and by those who worked under her and to whom she gave of her best. All who knew her will wish to extend their sympathy to her husband and their daughter and to her mother and sister.—W. M. G.

Medical Notes in Parliament

WORLD POPULATION AND FOOD SUPPLIES

Viscount SAMUEL invited the House of Lords on April 28 to consider the continuing and rapid increase in world population and the consequent need for increasing production of food and raw materials if living standards were to be maintained and improved.

He said that in 1850 the world population was rather over 1,000 million; to-day it was 2,500 million; and, if present trends were continued, by the early part of next century it would be 5,000 million. These figures had given rise to great anxiety, and the question was asked whether the human race was heading to sheer disaster. Dr. A. V. Hill said, in his presidential address to the British Association the year before last, that the rapid lowering of death rates all over the world meant that unless there was a deliberate restriction of birth rates in many countries there would be an inevitable fall in living standards.

The proposition that Lord Samuel put was that science, which had brought about the danger, brought also the means for preventing it, and that it was a fallacy to suppose that a mere increase of population must be a sheer liability. There were enormous opportunities for extending the areas of cultivation and vastly increasing the yields. Long-range possibilities included the development of nuclear energy, which might bring economic salvation to countries short of other sources of power; and the reaping of a greater harvest from the sea, including plankton, which for the next generation might be familiar as a main source of human food supply—it was only a question of the mode of preparation and availability. Plankton could be had for the asking; it contained millions of tons of proteins and quantities of vitamins. If the human race had been clever enough to grasp nitrogen out of the air and convert it by means of artificial fertilizers into bread and milk, surely it would be clever enough to take plankton from the sea and make it available in one form or another for human sustenance.

Lord BOYD-ORR said it was easy enough in theory to increase food, but not so easy in practice. In the Eastern countries—the food-deficit countries—there were social, religious, and economic difficulties. The food and economic problems might cancel each other out, because if food production was to be doubled an enormous increase in industrial equipment would be needed, and increased purchasing power and markets result from it.

The ARCHBISHOP OF YORK said that in asking the medical staffs of tropical hospitals what were the chief illnesses with which they had to deal, he had been struck that so often the answer had been, "With the exception of malaria, there is no particular tropical illness that causes us trouble, but the ordinary illnesses which you have at home are intensified and made more serious through malnutrition." He mentioned that one of the results of the eradication of malaria in British Guiana had been a decrease in infant mortality from 250 a thousand to 67 in a year, and the birth rate had also gone up. Birth control must be discussed and considered, but first things must be taken first, and he had found in the West Indies the opinion that the immediate need was to raise the standard of living, and that when that had been done people would have a greater appreciation of the necessity for parental responsibility.

Birth and Death Control

Lord BEVERIDGE said that what had been called "death control," the saving of lives through the development of science, had become one of the major factors in the world

population problem. It was clear that it automatically required birth control in some form or other.

Lord SIMON of Wythenshawe said that when this country started death control nearly 200 years ago medical and sanitary science was in its infancy. It took us nearly 200 years to get the death rate down to 40 a thousand. But recent inventions like penicillin and D.D.T. had produced remarkable results. If India, for example, applied Western health measures with comparable efficiency she would have an increase in population not of five million a year but ten million, and would not have time to get birth control going or industry developed. The Indian Government's five-year plan included, for the first time in history, he thought, the initiation of a campaign to limit the increase of population and as early as possible to stabilize it.

Lord HADEN-GUEST said that a world survey in much greater detail was required before any conclusions were drawn, and the necessity for control of the birth rate must be faced.

Lord STAMP said that as a medical microbiologist he was particularly interested in the contribution that research in the biological sciences might make. Further research was needed into the nutritive value of yeast for man and animals, and the methods of improving its palatability. Another group of organisms which appeared to have considerable potentialities as food was the algae, in particular the chlorella or green algae often seen as a green scum on the surface of ponds. These plants had high yields of fats and protein of nutritive value. There were many others which might prove of equal or greater value, and there was also the possibility of utilizing further the photosynthetic action of sunlight in building up proteins of nutritive value by devising methods for the extraction of proteins from leaves of plants that were at present largely wasted.

Earl DE LA WARR, for the Government, said the real problem was that agriculture must keep pace with medicine. It could do so only with a great effort. Birth control was primarily a matter for the countries concerned, and interference of that sort from this country would not be welcomed. He recounted the aid which was being given to the Food and Agriculture Organization and the United Nations technical assistance programme and through the Colombo plan. He agreed that the subject was one of great importance, and assured the House that the Government saw it as such and was prepared to do something as well as talk about it.

INQUIRY INTO HOMOSEXUALITY AND PROSTITUTION

It was announced in the House of Commons on April 29 that the Home Secretary, having given careful and anxious consideration to various representations that had been made on homosexual offences, and also close attention to the parallel problem of the law relating to prostitution and solicitation generally, had decided—in conjunction with the Secretary of State for Scotland—to appoint a committee to study both these questions.

Sir HUGH LUCAS-TOOTH, Under Secretary at the Home Office, added that he was anxious to secure the services of able and experienced men and women to serve on the committee, and therefore it might be some little time before he was able to announce the membership and terms of reference. The Home Secretary believed that a thorough investigation by a well-qualified body would throw useful light on the scope and nature of these difficult and controversial matters, and would make a valuable contribution to the problem of how the criminal law should deal with them.

Mr. DESMOND DONNELLY (Pembroke, Lab.) proposed the appointment of a Royal Commission to investigate the law relating to and the medical treatment of homosexuality, on the motion for the adjournment of the House. He said it was important that if such a commission was appointed it should look into the matter with a view to seeing what medical treatment could be provided. He was advised that this was not mainly a glandular problem; it was a psychiatric problem, and the answer could often be found in psychiatric treatment where this was possible, or more particularly in studying the treatment of young people in their nursery years, because that was the crux of the whole matter. A Royal Commission should go into the matter and see that there was widespread public knowledge of how this sort of thing could be avoided.

Sir ROBERT BOOTHBY (Aberdeenshire, East, Con.) said that all the laws relating to this subject were enacted before any of the discoveries of modern psychology, and in any event were out-moded. The duty of the State was to protect youth from corruption and the public from indecency and nuisance. What consenting adults did in privacy might be a moral issue between them and their Maker, but it was not a legal issue between them and the State. What were called infanto-homosexuals should be segregated unless and until they were cured—as indeed must all those who committed offences against children and young people of either sex. But to send confirmed adult homosexuals to prison for long sentences was not only dangerous but madness. The prisons in their present overcrowded condition were factories for the manufacture of homosexuality. Recent cases established the need for an authoritative inquiry to furnish Parliament with the necessary expert knowledge and guidance for appropriate legislative and administrative action.

Sir HUGH LUCAS-TOOTH, replying, said that three main questions had emerged: What was the prevalence of homosexual activities? What was the impact of the law on such activities, and was any amendment of the law desirable? And what could be done by way of curative treatment, apart from punishment, for those who offended? There were no reliable means for assessing the prevalence of homosexual practices, but it was right to say that there had been a serious increase. Between 1938 and 1952 indictable offences known to the police had increased between four- and five-fold. He thought it could be said with complete truth that the reasons for the increase were simply not known. There would be general agreement that the criminal law ought to provide effectively for the protection of the young and the preservation of public order and decency. The question was whether the law should confine itself to securing those two objects, or whether it should be amended to permit unnatural relations between consenting adults in private. Such activities were no crime in many countries.

What medical science could do for those prisoners who were willing and able to be helped by psychological treatment was done to-day. Visiting psychotherapists had been appointed at certain prisons. Elsewhere prison medical officers submitted to the Prison Commissioners the names of any prisoners serving substantial sentences whom they thought were likely to benefit by treatment from psychotherapists with a view to their transfer. There was a scheme for prisoners serving shorter sentences to be seen by visiting psychiatrists from regional hospital boards with a view to continued treatment after release. The Prison Commissioners proposed to build a special establishment for mentally abnormal prisoners, and sexual and homosexual cases would be included. But those who could benefit were in a minority.

Cancer Registration

Mr. S. AWBERY (Bristol, Central, Lab.) asked if the Minister of Health, as a means of combating cancer, would give powers to local authorities to register all persons suffering from this disease; and if he would promote schemes to educate patients through general practitioners and other means on the best form of treatment. Miss PAT HORNSBY-SMITH replied that hospital boards were encouraged to arrange for the registration of all cases treated in hospital, and to provide information about incidence and results of treatment. The Minister had already invited local authorities to promote educational schemes, in co-operation with hospital authorities and general practitioners.

Mr. AWBERY said that many people who suffered from the disease were afraid to go to their doctors in the initial stages, and asked if the Minister would carry on a campaign through medical officers of health to encourage people to see their doctors at a stage when they could be helped. Miss HORNSBY-SMITH said that she shared his concern. They were working on the advice of the standing advisory committee on cancer and radiotherapy, and carrying out a scheme recommended by them.

Emphysema Research

Sir JOCELYN LUCAS (Portsmouth, South, Con.) asked the Minister of Health on April 29 if he would set up a special centre for research into the cause and cure of emphysema, and if he would give an estimate of the number of sufferers affected. Miss PAT HORNSBY-SMITH said that research into the lung conditions with which emphysema was usually associated was in progress in a number of centres. There was not information available to form an estimate of the number of sufferers.

Sir J. LUCAS urged that, as neither the cause nor the proper cure of this complaint had yet been discovered, the Minister should do all he could to step up research, with a view to relieving sufferers. Miss HORNSBY-SMITH said that research into diseases of the lung was already carried out at such centres as Hammersmith, the Brompton Hospital, and Sheffield, which covered research into emphysema.

World Health Organization

Sir RICHARD ACLAND (Gravesend, Lab.) asked the Minister of Health on April 29 whether he would instruct the British Government to press for a substantial increase in the regular budget of the World Health Organization, and to pledge this country to pay its fair share in the increase. Miss PAT HORNSBY-SMITH stated that the proposed regular budget of the Organization for 1955 showed a substantial increase over that approved for 1954, but the Minister was not satisfied that this increase was justified. The matter would be further considered at the next World Health Assembly. The United Kingdom contributed to the budget on a scale approved by the Assembly.

Sir RICHARD ACLAND asked that Britain should press for an increase in the budget so that the Organization could overcome its many problems. Miss HORNSBY-SMITH : "Not unless we are satisfied that the increase is justified."

Mr. A. BLENKINSOP (Newcastle-upon-Tyne, East, Lab.) asked for an assurance that there would be a long-term guarantee of funds to the Organization so that it could recruit the technical and qualified staff urgently needed for long-term contract work. Miss HORNSBY-SMITH said that was a much wider question, which she could not possibly answer.

Hospital Private Beds

Mr. A. MOYLE (Oldbury and Halesowen, Lab.) asked the Minister of Health on April 29 what steps were taken to ensure that private beds were not reserved for the use of fee-paying patients when there were urgent or chronic cases on the general waiting-list. Miss PAT HORNSBY-SMITH replied that the National Health Service Act specifically provided for patients in urgent medical need of treatment to be admitted to a pay-bed without charge if no alternative accommodation was available. The Minister had brought this to the notice of hospital authorities, and had also asked them to ensure that pay-beds not in full use for private patients were used for other patients, whether urgent cases or not.

Mr. MOYLE asked what view the Minister took of the heavy fees paid by private patients for minor operations, like the removal of tonsils, for which they were able to get attention within a week, whereas children had to wait as long as six months. Miss HORNSBY-SMITH said she hoped he would not exaggerate these claims. In the hospitals in which he was interested the Minister had assured him that whereas 25 tonsillectomies were done in a week under the Health Service there were only four in a year on private fee-paying patients. If M.P.s had any evidence the Ministry would be glad to go into it to ensure that there was no abuse. It was not fair to suggest there was widespread abuse.

Medically Unfit for Service

Mr. IAN HARVEY (Harrow, East, Con.) was informed by Mr. HAROLD WATKINSON, Parliamentary Secretary, Ministry of Labour, on April 27, that it was estimated that 20% of the men medically examined on registering for national service in the first quarter of this year were not fit for service, on medical grounds. Mr. HARVEY said there was some concern about evasion of national service through men obtaining doctors' certificates, which were then honoured by the board, and asked that the matter should be looked into. Mr. WATKINSON said he did not think so. The medical boards did as the House had asked and were careful to see that they did not call up men who were medically unfit for military service. That sometimes meant delay in conferring with consultants, and so on, but he did not think many people evaded service for medical reasons. Mr. GEORGE THOMAS (Cardiff, West, Lab.) asked if the percentage was rising or falling, as 20% seemed a high figure for people unfit, and Mr. WATKINSON replied that it had been about the same over the past 12 months.

Antidotes to Poison

Lieutenant-Colonel W. SCHOFIELD (Rochdale, Con.) asked the Home Secretary if, where the law provided that any poisonous fluid or substance must be marked and labelled "poison," he would make it compulsory that the antidote to the poison should also be clearly stated. Sir DAVID MAXWELL FYFE replied on April 29 "No." The Poisons Board had advised against the introduction of such legislation. There were great dangers, because undue emphasis on antidotes might result in the loss of valuable time in obtaining medical help.

Contaminated Oranges.—Miss PAT HORNSBY-SMITH informed Mr. R. W. SORENSEN (Leyton, Lab.) on April 29 that the Ministry of Health had received no reports from medical officers of health or any general practitioner of intestinal or other ill effects suspected to be due to the contamination of oranges by thiourea.

Sanitary Inspectors.—The Minister of Health stated on April 29 that he and other Ministers concerned had considered the report of the working party on the recruitment, training, and qualification of sanitary inspectors, and he proposed to discuss it with the interested bodies with a view to implementing the working party's proposals. It should not be inferred that he necessarily accepted all the detailed recommendations of the working party.

Medico-Legal

AN UNCERTAIN WILL

[FROM A SPECIAL CORRESPONDENT]

A recent decision in the courts has been of great moment to the two principal medical charities, and is therefore of importance to the whole profession. A Miss X, daughter of a long-deceased doctor, made a will in which, after various bequests, including annuities to be paid by her executors to four female friends, she left the residue to be divided (not quite equally) between the Royal Medical Foundation of Epsom College and the Royal Medical Benevolent Fund. One of the legacies was a bequest of £250 to her usual medical attendant.

So far all was plain sailing, but shortly before her death she executed a codicil in which she empowered her executors at their discretion to allow her doctor to buy her house, should he want to do so, "not necessarily at its full probate value but for such an amount as he can afford." The house was valued for probate at £700 at the time when Miss X died, about two years ago. The doctor then offered the

executors £100 for the house. Both the charities, naturally enough, protested emphatically against the acceptance of this offer. Various attempts to arrive at a compromise solution of the dilemma broke down, so finally the executors sought the direction of the court on the course they should follow. The clause was declared to be void for uncertainty. For once the strict letter of the law and natural justice seem to have coincided, which, to laymen, does not appear always necessarily to be the case.

HYPNOTIST LECTURER ACQUITTED

Believed to be the first person to be prosecuted under the Hypnotism Act of 1952, Mr. D. T. Watson, aged 46, was acquitted at Northampton on April 28 on a summons brought under the Act.[1] Watson was a lecturer at a meeting arranged by the International Friendship League at a Northampton café, and he was accused of giving a public demonstration of hypnotism on a young man, a journalist, at a place which was not licensed for it. The Act says that "no person shall give an exhibition, demonstration, or performance of hypnotism on any living person at or in connexion with an entertainment to which the public are admitted," unless authorization has been given. The defence claimed that the lecture was not an entertainment, and that the purpose of the Act was to prevent the prostitution of hypnotism by people who wanted to make money from it in theatres. The magistrates were satisfied that the demonstration was not an entertainment.

[1] *Manchester Guardian*, April 29.

Universities and Colleges

UNIVERSITY OF OXFORD

In Congregation on January 21 the degree of B.M. was conferred on J. G. Bateman and B. C. Morson.

The Board of the Faculty of Medicine has re-co-opted Dr. A. M. Cooke and co-opted Dr. E. M. Buzzard for the statutory period of two years from the first day of Hilary Term, 1954.

UNIVERSITY OF ST. ANDREWS

The degree of M.D. has been conferred on Norman Levinson.

The following candidates have been approved at the examination indicated:

FINAL M.B., CH.B.—W. Chaplain, I. M. Sutherland, Mary E. Woods.

UNIVERSITY OF GLASGOW

The following degrees were conferred on January 16:

M.D.—J. Bruce (with commendation), Helen I. W. Kerr-Taylor, R. Lamb (with commendation), J. M. McBride (with high commendation), H. Thompson, R. M. L. Weir.

M.B., CH.B.—Florence M. D. McC. Adams, D. MacF. R. Adamson, W. G. Aitchison, J. A. H. Aitken, Elizabeth H. Arklie, W. G. Barbour, J. Bolland, Evelyn M. Borland, R. H. Boyd, Elizabeth J. B. Buchanan, J. M. Cameron, W. S. Campbell, J. A. Chapman, W. H. Cochrane, J. A. Dand, W. A. Dawson, Marion R. H. Donald, R. G. Dryden, D. Duncan, Stella E. G. Gibson, Katherine M. Girdwood, A. I. M. Glen, I. B. Hall, Margaret A. Hart, G. S. Henderson, M. Holmes, G. M. Jesner, J. H. Lawrie, Myra Leatham, W. J. Leishman, E. S. Livingstone, Isobel McClung, G. T. MacCulloch, A. McCutchion, A. J. McDonald, I. G. MacFarlane, J. A. McCarry, W. G. MacIntosh, J. C. MacIntyre, A. Mackintosh, Marion T. McKissock, J. S. MacLean, J. H. McLean, J. D. Mabon, W. Mitchell, R. S. Moir, J. B. Morris, J. M. Neilson, J. M. Newton, R. A. H. Newton, W. A. Nicol, G. H. Parker, A. Patrick, Flora K. Prentice, Euphemia Quigley, Helen A. Ritchie, A. Robertson, J. T. Robertson, A. W. B. Russell, I. D. Sanderson, R. W. Sharp, I. R. Sherret, C. E. Simpson, N. J. Skelton, W. D. Smith, W. McA. Speirs, D. A. Stalker, Doreen Steel, Anne M. Stewart, Jean O. Struthers, Margaret A. Timmins, P. G. M. G. Walker, Margaret Wallace, A. S. Wilson, W. Young.

UNIVERSITY OF LONDON

D. P. Walther, M.R.C.S., L.R.C.P., L.D.S. R.C.S., senior hospital dental officer, orthodontist in charge of the orthodontic clinic department at the Eastman Dental Hospital, and senior hospital dental officer at the Hospital for Sick Children, has been appointed to the University Readership in Orthodontics, tenable at the Royal Dental Hospital of London School of Dental Surgery.

UNIVERSITY OF SHEFFIELD

Dr. J. Wilkie has been appointed part-time Lecturer in Radiodiagnosis.

UNIVERSITY OF BRISTOL

The following candidates have been approved at the examinations indicated:

M.D.—J. D. Sheward.

FINAL M.B., CH.B.—P. B. Bailey, M. J. Betty, G. A. Bond, M. Ll. Cox, R. W. Digby, R. D. Doyle, R. I. Eastwood, Monica M. Gurnhill, K. W. Moulding, A. E. Nesling, T. F. J. Parker, W. E. Smith, D. G. Trott (with distinction in public health), R. Winstone. *In Group I completing the examination:* J. P. Bishop, Christine F. Boulter, Margaret V. Brown, J. Roylance, Catherine M. Stephen. *In Group II only:* K. G. Collins, Janet H. Keevil, E. C. Skeens.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—*Part II:* L. W. Bowen, D. E. Jarman, S. Prus.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on December 10, 1953, with Sir Reginald Watson-Jones, Vice-President, in the chair, Dr. Fred W. Rankin, President of the American College of Surgeons, was awarded an Honorary Fellowship.

Hunterian Professorships were awarded to Mr. R. C. Evans, and Dr. Michael Ward for a lecture on "The Ascent of Mount Everest—Medical Studies."

The Begley Prize was presented to Margaret M. Heley (Royal Free).

It was decided to proceed at once with the building of the Nuffield College of Surgical Sciences.

Diplomas of Fellowship were granted to the following candidates: J. A. James, K. L. Barnes, C. M. Phillips, R. B. McGrigor, D. B. Moffat, R. M. Harvey, G. F. Hird, J. S. J. Morley, J. E. Oliver, L. G. Fison, K. Till, A. S. Falconer, A. E. Flatt, R. A. Daws, J. A. G. Holt, Betty M. L. Underhill, J. Bihari, P. B. Foxwell, S. Panikkar, B. G. Reynolds, Agnes R. D. Bartels, J. A. Snyder, K. S. E. MacRae, Margery Scott-Young, C. J. S. Sergel, M. Shaffi, G. C. Pritchard, K. G. Malcomson, J. M. Ellis, I. M. Grant, H. D. W. Powell, F. H. Gamali, J. D. Glanville, W. Grundill, P. A. P. Joseph, A. M. Akram, A. Benjamin, R. F. Burton, J. K. Craig, W. S. Foulds, P. E. Ghadiali, B. Goldman, R. J. Hart, K. W. Hinrichsen, G. S. Karai, J. S. Lekias, Elaine Lister, E. A. McVerry, K. D. J. Vowles, K. H. Abdel-Ghaffar, A. K. Das, I. Sober, J. B. R. Wells, C. G. Wilson, W. S. Wilson, F. J. Hall, H. C. Jones, J. Kiely, B. V. Kyle, E. D. McIntyre, S. A. Mellick, D. J. Retief, J. E. S. Scott, N. J. Way, R. F. Zacharin, A. F. G. Anderson, R. R. Barnett, J. G. Brice, A. F. Ferguson, H. R. McCoy, M. K. Mehra, A. G. Morgan, P. J. Mortensen, G. T. Smedley, T. K. Thorlakson, M. Wynyard, J. Chalmers, D. Davies, L. R. De Jode, E. S. P. Ferguson, R. S. Gupta, C. H. Maclaurin, B. Shandling, K. K. Sinha.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

The following were admitted to the Membership of the College on February 5: K. H. Anderson, E. E. Doyle, K. C. Finkel, L. G. McElearney, M. F. McParland, J. B. O'Dullivan.

SOCIETY OF APOTHECARIES OF LONDON

The diploma of L.M.S.S.A. has been granted by examination to the following successful candidates: J. M. Goyder, T. J. Gallivan, I. Dollond, T. J. Taylor, T. G. Wadsworth, E. Dayan, J. Curtis, J. K. Anderson, J. G. Robertson, M. W. L. Davis, B. Clarke.

The following candidates have been awarded the Diploma in Industrial Health: W. R. Brown, S. Chakravorti, K. P. Duncan, B. K. Ghose, R. Makin, P. B. Nicol, J. D. Pickford, M. K. Qureshi-Ul-Hashmi, A. W. W. Robinson, T. Simpson, H. Stott.

APOTHECARIES' HALL OF IRELAND

At recent examinations the following candidates received the diploma of L.A.H. Dublin: S. M. Abba, E. Allan, A. Azike, J. F. L. Barry, Evelyn Blake, E. W. Burke, D. R. Chiney, G. G. Dibue, P. P. Gallagher, W. H. Hamilton-Deane, P. J. A. Horan, J. M. Langan, Chew Seng Lau, J. M. Mangan, Erminie Marazzi, D. Martin, Bridget Moylan, P. D. Moylan, H. McCarthy, O. L. McGuinness, D. C. O'Sullivan, Maire Quigley, J. A. Quigley, T. F. Regan, Constance Strickland, J. D. Steele, T. E. Winckworth, R. Whyte.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **April 17** (No. 15) and corresponding week 1953.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	14	1	3	1	0	18	2	8	0	
Dysentery	919	121	273	4	3	282	33	88	6	
Encephalitis, acute	2	0	0	0		3	0	0	0	
Enteric fever:										
Typhoid	1	1	0	0	0	2	0	0	0	
Paratyphoid	5	0	0	0	0	7	0	1(A)	0	
Food-poisoning	88	9		6		56	9		0	
Infective enteritis or diarrhoea under 2 years				12	14				21	19
Measles*	1,912	67	144	92	281	18,861	835	550	269	284
Meningococcal infection	24	1	18	1	2	54	6	11	1	4
Ophthalmia neonatorum	35	4	12	0		48	1	4	0	
Pneumonia†	451	17	185	10	0	796	57	473	14	8
Poliomyelitis, acute:										
Paralytic	10	0	3	0	3	26	1	1	0	2
Non-paralytic	7	1				8	0			
Puerperal fever§	185	24	14	0		208	30	23	1	
Scarlet fever	994	60	137	38	29	994	67	151	35	51
Tuberculosis:										
Respiratory	751	95	168	32				147	27	
Non-respiratory	111	9	20	2				16	6	
Whooping-cough	1,980	69	248	37	19	2,847	181	374	40	152

DEATHS in Great Towns	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0		0
Dysentery	0	0		0		0	0			
Encephalitis, acute		0	0		0					0
Enteric fever	0	0	0	0		0	0	0		
Infective enteritis or diarrhoea under 2 years	7	0	0	2	3	8	1	1	3	0
Influenza	6	1	1	1	0	37	1	1	2	3
Measles		0	0	0	1		0	0		2
Meningococcal infection		0	2				0	0		
Pneumonia	189	26	22	8	4	300	33	26	19	11
Poliomyelitis, acute	0	0			0	8	1			0
Scarlet fever		0	0	0	0		0	0		0
Tuberculosis:										
Respiratory	90	10	10	0	6	119	19	14	4	6
Non-respiratory			1	0	3		2	2	3	3
Whooping-cough	2	0	0	0	1	3	0	1	0	1
Deaths 0–1 year	218	29	42	8	10	229	30	34	14	22
Deaths (excluding stillbirths)	5,092	703	577	129	178	5,428	731	623	126	209
LIVE BIRTHS	6,339	955	769	261	311	8,068	1175	923	235	409
STILLBIRTHS	206	21	24			196	25	20		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Hospital In-patient Statistics

A further contribution to the study of morbidity statistics published this week includes figures of cases admitted to certain hospitals in England and Wales in 1949 analysed by sex, age, disease, length of stay, and social class.[1] The volume also includes some figures from wartime E.M.S. hospital records. The significance of many of the figures tabulated is not easy to interpret, because the population at risk is problematical. Hospital administrators, however, may find useful guidance on the proportions in which groups of beds should be set aside for different diseases. Some of the sex ratios of disease incidence obtainable may usefully be compared with those obtained from mortality statistics. Table H2 shows that the average stay in hospital is lower in the provincial teaching hospitals than in either the London teaching hospitals or the regional board hospitals. The figures for the last-named are influenced by the relatively high proportion of old people admitted.

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in March, 1954, was 118, compared with 114 in the previous month and 122 (revised figure) in March, 1953.

The number of cases of industrial diseases in the United Kingdom reported during March was as follows: lead poisoning 2, other poisoning 0, anthrax 4, epitheliomatous ulceration 12, and chrome ulceration 27; total 45. There was 1 death from epitheliomatous ulceration.—*Ministry of Labour Gazette*, April, 1954.

Venereal Diseases

In England and Wales during the quarter ending December 31, 1953, 1,557 new cases of syphilis were reported as attending the clinics. Of these, 276 were classified as primary, secondary, or latent in the first year of infection. 24 cases of congenital syphilis in children aged under 1 year were reported, and 213 cases in persons over that age. New cases of gonorrhoea numbered 4,697, of chancroid 83, and of non-gonococcal urethritis (males only) 3,253.—*Monthly Bulletin of the Ministry of Health*, April, 1954.

Infectious Diseases

The incidence of infectious diseases fell in England and Wales during the week ending April 17. The largest declines in the number of notifications were 635 for dysentery, from 1,554 to 919, 482 for whooping-cough, from 2,462 to 1,980, 381 for measles, from 2,293 to 1,912, and 380 for scarlet fever, from 1,374 to 994.

A decrease in the incidence of scarlet fever was recorded in most areas; the largest falls were Lancashire 30, from 166 to 136, Durham 24, from 44 to 20, and Derbyshire 21, from 31 to 10. The largest declines in the number of notifications of whooping-cough were 92 in Yorkshire West Riding, from 259 to 167, 54 in Norfolk, from 83 to 29, and 47 in Lancashire, from 237 to 190, while the only rise of any size was 36 in Gloucestershire, from 39 to 75. 14 cases of diphtheria were notified, being 2 more than in the preceding week. The largest falls in the notifications of measles were 119 in Staffordshire, from 334 to 215, 92 in Lancashire, from 499 to 407, and 45 in Cheshire, from 132 to 87, and the largest rise was 43 in Durham, from 65 to 108. 3 of the 5 cases of paratyphoid fever were notified in Anglesey, Beaumaris M.B.

17 cases of acute poliomyelitis were notified. These were 3 more for paralytic and 4 more for non-paralytic cases

[1] *Registrar-General's Statistical Review of England and Wales for the Year 1949: Supplement on the Hospital In-patient Statistics.* H.M.S.O., 15s.

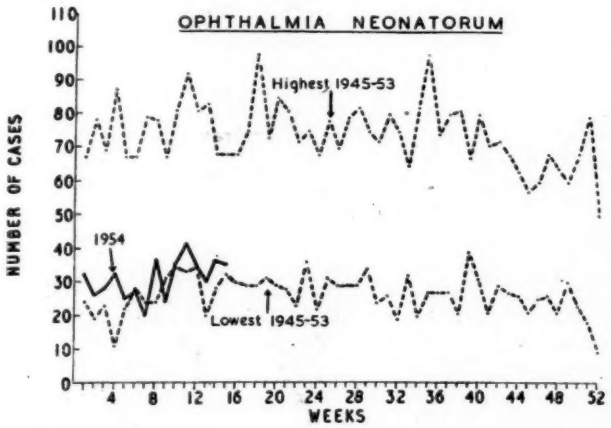
than in the preceding week. 3 cases were notified in Somersetshire and 2 in each of the counties of Devon, Warwick, Lancashire, and Yorkshire East Riding.

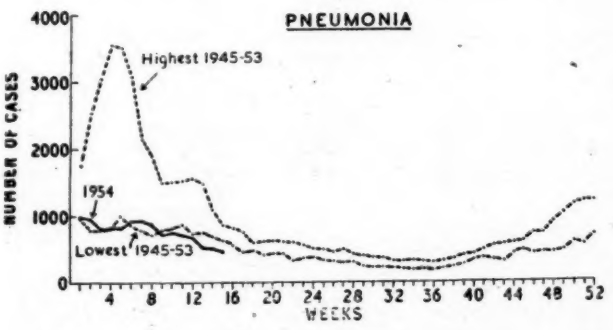
The largest returns of dysentery were Yorkshire West Riding 148 (Sheffield C.B. 42, Dewsbury C.B. 18, Leeds C.B. 17, Bradford C.B. 10, Wortley R.D. 10), Lancashire 133 (Salford C.B. 22, Liverpool C.B. 15, Bolton C.B. 11), London 121 (Islington 42, Lewisham 17, Wandsworth 15), Leicestershire 88 (Leicester C.B. 83), Middlesex 48 (Edmonton M.B. 12, Willesden M.B. 11), Nottinghamshire 40 (Nottingham C.B. 32), Essex 31, Norfolk 28 (Norwich C.B. 26), Gloucestershire 27 (Bristol C.B. 24), Warwickshire 26 (Birmingham C.B. 23), Kent 25, Staffordshire 23 (Cannock U.D. 15), and Surrey 22 (Croydon C.B. 17).

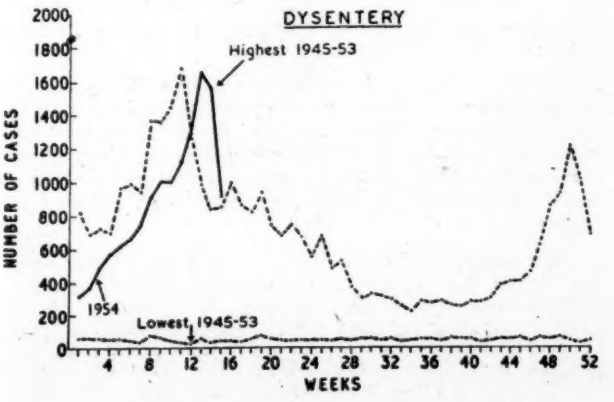
In Scotland the largest returns of dysentery were 147 in Glasgow, 40 in Lanark county, and 39 in Edinburgh.

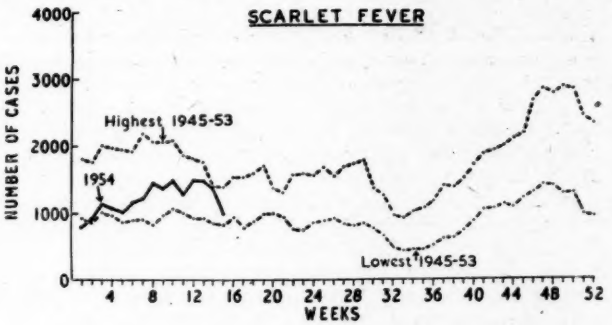
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1945–53 are shown thus - - - - - - -, the figures for 1954 thus ————. Except for the curves showing notifications in 1954, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending April 24

The notifications of infectious diseases in England and Wales during the week included pneumonia 478, scarlet fever 789, whooping-cough 2,133, diphtheria 12, measles 2,196, dysentery 711, acute poliomyelitis 10, paratyphoid fever 3, and typhoid fever 1.

Not Smallpox

A Briton who returned by air from Spain on April 24 developed a rash which was reported to have aroused suspicion of smallpox, but further observation has excluded this diagnosis.

Medical News

World Health Assembly.—The seventh World Health Assembly opened in Geneva on May 4.

Clinical Science Institute at Belfast.—The most ambitious extension to Queen's University, Belfast, since its foundation in 1845 is the Institute of Clinical Science which was opened on May 7. It comprises two buildings on the hospitals site at Grosvenor Road, Belfast, which are directly linked with each other and with the adjacent Institute of Pathology and the Royal Victoria Hospital. Other hospitals in the vicinity are the Royal Maternity Hospital, the Royal Belfast Hospital for Sick Children, and the Musgrave Clinic. The new Institute will house the departments of medicine, surgery, therapeutics, obstetrics and gynaecology, child health, and social and preventive medicine, and one for research. In addition there are a medical library, lecture and reading rooms, operating rooms, laboratories, a photographic studio, and workshops. The design of the research department has been based on that at the Mayo Clinic in America. It is expected that the Institute will provide magnificent facilities for both undergraduate teaching and postgraduate research.

Nuffield Scottish Committee.—The first meeting of the Scottish Advisory Committee of the Nuffield Provincial Hospitals Trust was held in St. Andrew's House, Edinburgh, on April 28, with Sir George H. Henderson in the chair. The new committee will advise the trust on applications for grants towards projects in which either the Trust or the Nuffield Foundation may be interested. The medical members of the committee are Dr. May D. Baird, Mr. P. Martin Brodie, Professor Thomas Ferguson, Professor Ian G. W. Hill, and Professor C. F. W. Illingworth.

Eugenics Quarterly.—The American Eugenics Society has commenced publication of *Eugenics Quarterly*, which replaces *Eugenical News* as the official organ of the Society. Subscription to *Eugenics Quarterly* is $3 per annum.

British Association of Physical Medicine.—The annual meeting was held on April 30 and May 1 at King's College Hospital Medical School, London, by kind permission of the Dean. The opening session was devoted to a discussion on "The Scientific Approach to Physical Medicine," the

principal speakers being Dr. A. C. Boyle, Dr. A. J. Richardson, and Dr. Richard Doll. Each of them emphasized the vital necessity of applying rigid statistical criteria before any new form of physical treatment was accepted. Failure to "control" clinical impressions in the past had led to much empirical therapy, the scientific basis of which was now being challenged. Subsequent speakers stressed some of the ethical and technical difficulties in carrying out an impeccable clinical trial. The second morning session took the form of a conference on industrial and social rehabilitation, organized by Dr. F. Cooksey, in which twelve illustrative cases were discussed by medical staff, almoner, occupational therapist, local disablement resettlement officer, and other interested officials. On one of the afternoons a clinical meeting was held, and on the other short papers were read. The annual dinner was held at the Grosvenor House, with Lord Horder presiding. The toasts were given by the Minister of Health (Mr. Iain Macleod), Lord Horder, Dr. A. C. Boyle, and Sir Cecil Wakeley, P.R.C.S.

Medical Women's Federation.—Dr. Annis Gillie has been elected president of the Medical Women's Federation. Her induction by the retiring president, Dr. Mary Esslemont, was announced as the final ceremony at the annual general meeting held on May 6 at Sheffield. The title of Dr. Gillie's presidential address was "Motive and Momentum."

Hunterian Society.—Dr. W. S. C. Copeman has been elected president of the Hunterian Society of Great Britain in succession to Sir Heneage Ogilvie.

Smokeless Zone for Bolton.—The Minister of Housing and Local Government has approved an Order creating the first smokeless zone in Bolton. The zone is an area of 86 acres in the centre of the city. The Order will come into force on November 1.

Professor Otto Loewi, the distinguished German pharmacologist, who now lives in New York, has been made a Foreign Member of the Royal Society. In 1936 Professor Loewi shared a Nobel Prize with Sir Henry Dale for their work on the transmission of nerve impulses.

Sir Landsborough Thomson, second secretary of the Medical Research Council, has been elected president of the Zoological Society of London.

Dr. J. W. Landells has been appointed to the University readership in morbid anatomy tenable at the London Hospital Medical College.

COMING EVENTS

Cavendish Lecture.—Lieutenant-General Sir William MacArthur will speak on "Pepys and the Plague" on May 10 at 8.30 p.m. at the Royal Society of Medicine, 1, Wimpole Street, London, W.1.

Medical Association for the Prevention of War.—A public conference will be held on May 15 from 2.30 to 5.45 p.m. at 45, Russell Square, London, W.C.1. The theme of the meeting is "The Concept of Race," and the speakers will include Professor Lionel Penrose, F.R.S., Dr. N. A. Barnicot, Mr. E. S. Sachs, and Dr. Duncan Leys.

William Blair-Bell Memorial Lecture.—Dr. Ian Donald will lecture on "Atelectasis Neonatorum" on May 21 at 5 p.m. at the Royal College of Obstetricians and Gynaecologists, 58, Queen Anne Street, London, W.1. Admission is by ticket only, obtainable from the secretary of the College.

Bristol Medical Exhibition.—The exhibition will be held at the Victoria Rooms, Bristol, from May 17 to 21 from 11 a.m. to 6.30 p.m. daily (7.30 p.m. on May 19). It will be officially opened at 11.30 on May 17 by Professor C. Bruce Perry. It is expected that the film of the Siamese twins operation will be shown in each day's programme. Further information may be obtained from the organizer of the exhibition, Victoria Rooms, Bristol.

Meeting of American College of Surgeons in London.—The American College of Surgeons is holding a three-day sectional meeting at the Royal College of Surgeons, Lincoln's Inn Fields, on May 17, 18, and 19. The programme for the meeting has been prepared by the American College on the lines of one of their typical sectional meetings, while the local arrangements are in the hands of the Royal College. The American College of Surgeons has issued invitations to all Fellows of the Royal College of Surgeons and to all members of the Association of Surgeons of Great Britain and Ireland. The programme is as follows:

Monday, May 17

9.00–12 noon.	The Great Hall, Royal College of Surgeons: Film and Lectures.
12.15–2.15 p.m.	Luncheon and Panel Discussion on: "Intestinal Obstruction," at the Connaught Rooms, Great Queen Street.
2.30 p.m.–6.00 p.m.	The Great Hall, Royal College of Surgeons: 2.30 p.m., Symposium on Gynaecology. 3.20 p.m., Panel Discussion on: "Pre- and Post-operative Care." 5.00 p.m., Presentation of Honorary Fellowship. 5.05 p.m., Hunterian Lecture on: "Progressive Exophthalmos."
6.30 p.m.–7.30 p.m.	Various Receptions.
9.30 p.m.	Reception by President and Council at Royal College of Surgeons.

Tuesday, May 18

9.00 a.m.–12 noon	The Great Hall, Royal College of Surgeons. Symposium on: "Cardiovascular Surgery." Room I, Royal College of Surgeons. Symposium on: "Cancer."
2.00 p.m.–6.00 p.m.	Visits to London Hospitals.
7.30 p.m. for 8.00 p.m.	Banquet at the Dorchester Hotel, Park Lane.

Wednesday, May 19

9.00 a.m.–12.20 p.m.	The Great Hall, Royal College of Surgeons: Film and Lectures.
9.00 a.m.–12.15 p.m.	Special Programmes for otolaryngologists and urologists at the Royal College of Surgeons, and for ophthalmologists at the Institute of Ophthalmology, Judd Street, W.C.1, and Moorfields Westminster and Central Eye Hospital.
12.35 p.m.–2.30 p.m.	Luncheon and Panel Discussion on: "Massive Gastrointestinal Tract Haemorrhage," at the Connaught Rooms, Great Queen Street.
2.45 p.m.–5.30 p.m.	The Great Hall, Royal College of Surgeons: 2.45 p.m., Moynihan Lecture on: "Pancreatitis, Fundamental and Clinical Aspects." 3.45 p.m., Expression of Appreciation. 3.55 p.m., Panel Discussion on: "Hand Surgery."

Newsholme Lectures.—Professor W. M. Frazer will deliver three lectures on "State Medicine in the Nineteenth Century" at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1, on May 24, 25, and 26 at 5.15 p.m.

Demonstrations for Consultants on Modern Aspects of Thyroid Disease.—A week's course will be held at the Postgraduate Medical School, Ducane Road, London, W.12, from September 20 to 24. Further details are given in our advertisement columns at page 40. Applications for places, which are limited to 40, should be made to the Dean before September 1.

American Geriatrics Society.—The eleventh annual meeting will be held at the Hotel Fairmont, in San Francisco, from June 17 to 19. Dr. Laurance W. Kinsell, Highland Alameda County Hospital, 2701, Fourteenth Avenue, Oakland 6, California, is in charge of arrangements for the meeting.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Monday, May 10

MEDICAL SOCIETY OF LONDON.—8.30 p.m., second general meeting. Annual Oration by Mr. G. L. Keynes: Second (and Third) Thoughts on the Surgery of the Thymus Gland.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Royal Society of Medicine, 8.30 p.m., Cavendish Lecture by Lieutenant-General Sir William MacArthur: Pepys and the Plague.

Tuesday, May 11

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, annual dinner.

EDINBURGH UNIVERSITY.—At Surgery Lecture Theatre, University New Buildings, 5 p.m., Second Sir John Fraser Memorial Lecture by Dr. Evarts A. Graham (American College of Surgeons): Cancer of the Lung, with Special Emphasis on the Aetiology.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. O. Oliver: Antibiotics.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Croonian Lecture by Dr. J. F. Smith: Nutrition and Child Health.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—3.45 p.m., Imperial Cancer Research Fund Lecture by Dr. L. M. Franks: Latent Carcinoma.

WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY.—5 p.m., Almroth Wright Lecture by Professor P. B. Medawar, F.R.S.: Wound Healing, with Special Reference to the Skin.

Wednesday, May 12

DUBLIN UNIVERSITY.—At Physiology Theatre, 4.30 p.m., John Mallet Purser Lecture by Professor E. B. Verney, F.R.S.: Water Diuresis.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. A. Dudgeon: Virus Diseases.

INSTITUTE OF ORTHOPAEDICS.—At Brockley Hill, Stanmore, 8 p.m., senior clinical pathological conference.

OXFORD UNIVERSITY.—At Physiology Theatre, 12 noon, Professor Z. M. Bacq (Liége): Actions of Cysteamine and Cystamine.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., Dr. G. W. B. James: lecture demonstration in psychiatry.

Thursday, May 13

ALFRED ADLER MEDICAL SOCIETY.—At 11, Chandos Street, W., 8 p.m., Dr. Franklin Bicknell: Diet and Behaviour.

FACULTY OF HOMOEOPATHY.—5 p.m., Dr. Pierre Schmidt (Geneva): Hidden Treasures of the Last Organon.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. A. Dudgeon: Virus Diseases.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Professor M. L. Rosenheim: Treatment of Nephritis.

ROYAL EYE HOSPITAL.—5 p.m., Mr. H. B. Jacobs: Relation of Nasal and Ocular Diseases.

ST. ANDREWS UNIVERSITY.—At Physiology Department, Dundee, 5 p.m., Dr. R. W. G. Wyckoff: Use of the Electron Microscope in Biology and Medicine.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., psychiatry demonstration by Dr. M. A. Partridge.

SURREY INTER-HOSPITAL PSYCHIATRIC ASSOCIATION.—At Roffey Park Rehabilitation Centre, Horsham, Sussex, 5.30 p.m., clinical meeting. Papers by Dr. V. W. Wilson, Dr. L. S. Davies, and Dr. T. M. Ling.

Friday, May 14

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. P. F. Borrie: Vascular Anomalies.

LEEDS UNIVERSITY.—At Riley Smith Hall, University Union, 3.30 p.m., Moynihan Lecture by Dr. A. Blalock (Baltimore, U.S.A.): Expanding Scope of Cardiovascular Surgery.

LONDON UNIVERSITY.—At Anatomy Lecture Theatre, University College, 5.30 p.m., special university lecture in psychology by Dr. M. Ray Denny (Michigan): Learning Theory and Experimental Extinction.

PAPWORTH VILLAGE SETTLEMENT.—At 26, Portland Place, London, W., 5 p.m., Fourth Varrier-Jones Memorial Lecture by Dr. H. G. Trimble (California, U.S.A.): Current Therapy in Pulmonary Tuberculosis.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Mr. E. P. Brockman: Disabilities of the Foot; 4 p.m., Professor R. B. Hunter: Control of Anticoagulant Therapy in Myocardial Infarction.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., Mr. L. H. W. Williams: Obstetric/Gynaecological Conference.

SOCIETY OF MEDICAL OFFICERS OF HEALTH: WELSH BRANCH.—At B.M.A. House, 195, Newport Road, Cardiff, 6.30 p.m., annual meeting.

Saturday, May 15

ASHTON, HYDE, AND GLOSSOP HOSPITAL MANAGEMENT COMMITTEE.—At Physiotherapy Department, Lake Section, Ashton-under-Lyne General Hospital, 2.30 p.m., clinical meeting.

BIOCHEMICAL SOCIETY.—At Department of Physiology, The University, Bristol, 11 a.m., 329th meeting, scientific papers.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Heyland.—On April 2, 1954, at the London Hospital, London, E., to Joanna (formerly Poynton), and Dr. Ralph Heyland, of Hermon House, Faversham, Kent, a son.

Mather.—On April 15, 1954, at Ashmount, Londesborough, York, to Dr. Maud (formerly Buchanan), wife of Dr. John S. Mather, a daughter.

O'Brien.—On April 27, 1954, at Leeds, to Elizabeth (formerly Craig), M.B., B.Chir., wife of Richard O'Brien, Wakefield, a brother for Alison—David Charles.

MARRIAGES

Fleischl—Quinton.—On May 1, 1954, at St. Paul's, Portman Square, London, W., Peter Fleischl, M.B., Ch.B., of Wellington, New Zealand, to Charmian Quinton, M.B., B.S., of London, W.

DEATHS

Fitter.—On April 1, 1954, Clara Ann Shipley Fitter, M.D., late of Streatham, London, S.W., and Hindhead, Surrey, aged 93.

Starforth.—On March 31, 1954, in hospital, William Percy Starforth, M.B., Ch.B., of London, S.E., formerly of Durham.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Vaccine Trial in General Practice

Q.—*I am aware of the recent Medical Research Council trials of whooping-cough vaccines, but I want to test for myself over a period of years the efficiency in general practice of a combined diphtheria–pertussis prophylactic. My difficulty is to find a suitable control group with which to compare my results. What control group would you advise?*

A.—It is difficult to see how a satisfactory trial of such a vaccine could be conducted in a general practice nowadays, it being presumed that the doctor is bound to vaccinate any child whose parents request it. The vaccinated children will form a "volunteer" group, and their home background, the size of family they come from, and other factors may make their risk of exposure to infection different from any "non-volunteer" control group. It might be of interest, however, to keep careful records of every occasion in which pertussis occurs in the vaccinated child's own family. An unvaccinated child of pre-school age without a known history of pertussis infection probably runs an 80% risk of himself becoming infected in such circumstances. With efficient vaccines this *secondary attack rate* is reduced to about 10%.

I am not optimistic that within the bounds of one practice the questioner will be able to collect sufficient data to calculate these secondary attack rates. Only-children will rarely be of use to him, and even if efficient vaccines have not been widely used in his area the brothers and sisters of children offered for vaccination will often have been vaccinated already.

Infection from the Chalice

Q.—*In certain churches the chalice at Holy Communion is passed from person to person. What are the risks of infectious diseases being spread by this means?*

A.—Scattered observations dating back to the last century have been made on this subject, although none of them are fully conclusive by modern standards, and authors who condemn the use of the chalice as insanitary do not appear to have been free from bias against the practice itself. Burrows and Hemmens,[1] who review this evidence and describe what appears to be the only recent study of the subject, begin by emphasizing that they "are concerned with neither the theory of the sacrament nor the relative ecclesiastical merits of the various methods of its administration."

A superficial resemblance between this problem and that of "sanitizing" drinking utensils in general leads them to point out that "ordained clergymen are highly educated persons whose administration of the sacrament would appear hardly comparable to the activities of the usual soda fountain employee, restaurant dish washer, or bar keeper." The hygienic precautions taken are described as "rotation of the chalice so that successive persons do not drink from the same place, and the wiping of the chalice both inside and out before the same place is used again, with a purificator or a series of purificators which are freshly laundered and ironed prior to use." It is also pointed out that in the Book of Common Prayer the directions for Communion of the Sick read ". . . the Minister shall first receive the Communion himself, and after minister unto those who are appointed to communicate with the sick, and last of all to the sick person."

These authors' actual experiments consisted in contaminating the rim of a silver chalice either with sterilized saliva to which pure cultures of various bacteria had been added or by drinking from it with or without an indicator organism

(*Chr. prodigiosum*) in the mouth, and studying the fate of the bacteria so deposited by subsequent quantitative culture. Silver is itself bactericidal, and a rapid fall in the numbers of bacteria recoverable was observed in comparison with their behaviour when similarly deposited on a glass slide. Moreover, the wiping of a smooth surface with a fine linen fabric mechanically removes anything deposited on it with a high degree of efficiency, and reductions in bacterial counts of 90% were observed to result from this process alone. From these and other experiments the authors were satisfied that the risk involved is very small, and it is said that in fact no instance of the transmission of infection by this means has ever been substantiated. Their least satisfactory evidence concerns *Myco. tuberculosis*. Experiments with this species were not quantitative, and were concerned only with survival on the surface of the chalice without wiping, but all guinea-pig tests up to 40 minutes after contamination were positive.

REFERENCE

[1] *J. infect. Dis.*, 1943, **73**, 180.

Idiosyncrasy to Procaine

Q.—*Following a subcutaneous injection of 5 ml. 2% procaine, a pregnant woman had a severe reaction which came on within 10 minutes and lasted for half an hour. It consisted in tachycardia and collapse. No adrenaline was given with the procaine. What is the nature of this reaction, and can the diagnosis be confirmed by patch test or other means? If the diagnosis is confirmed, can the patient be desensitized to procaine, or are there other local analgesics that may safely be used?*

A.—True allergic reactions to procaine usually manifest themselves as a local dermatitis to direct contact with the drug or urticaria and angioneurotic oedema from injections. The present reaction is due to the toxicity of the drug—that is, it is an idiosyncrasy rather than an allergy. The diagnosis cannot be confirmed by patch tests, but the reaction could be reproduced on further injections. Desensitization is thus not to be expected and I have not seen it reported. It is quite possible that a patient may show toxic reactions to procaine and have no reactions to such drugs as stovaine or supercaine which do not contain a para group. Buff[1] has found that a subcutaneous or intravenous dose of 0.5 to 1 mg. neostigmine methylsulphate will prevent collapse and dramatically reduce the cardiac rate to normal in cases with a toxic procaine tachycardia.

REFERENCE

[1] *Amer. Practit.*, 1950, **1**, 347.

Sodium Glutamate in Food

Q.—*Sodium glutamate seems to be a frequent constituent of the prepared foodstuffs being imported into this country, and recently in an American method of cooking rice it was recommended as an addition. It is said to be used as a condiment in the East, but I wonder if it has any other value in the cooking of rice and if it is entirely innocuous?*

A.—Sodium glutamate is usually made from wheat gluten by acid hydrolysis followed by neutralization with soda, but it can also be obtained as a by-product in the sugar beet industry. It is favoured as a means of obtaining a strong meaty flavour from cheap vegetable sources. Under the name "aginomoto" it is used extensively in Japan and China. It is very effective in reinforcing the taste of chicken in dishes consisting mainly of rice. Food manufacturers use it to improve the taste in canned and dehydrated meats. There is no evidence that it is harmful, and it is presumably metabolized in the same way as glutamic acid eaten in combined form in ordinary foods.

Stability of Antibiotics

Q.—*How stable are the commoner antibiotics in the refrigerator and at room temperature?*

A.—A full answer to this question occupies 12 pages and constitutes Chapter 4 of *Antibiotics: A Survey of their Properties and Uses*, London: Pharmaceutical Press, 1952, to which the inquirer is referred for details. The question presumably refers to solutions, and the stability of these depends not only on the temperature at which they are held, but on other factors such as *p*H. For example, penicillin is most stable at *p*H 6.0, and, if the trouble is taken to buffer the solution at this *p*H, it will last longer.

The only antibiotic so unstable as to cause serious difficulty is aureomycin: solutions of this for laboratory purposes should be made daily. Streptomycin, chloramphenicol, and terramycin are more stable than penicillin, and any of these four will suffer no significant loss of potency in one month or more if the solution is frozen, or in one week at about 4° C. These times may be extended if a loss of potency of the order of 10% is of no consequence.

NOTES AND COMMENTS

Drugs for Hypertension in Pregnancy.—Mr. JOHN SOPHIAN (London, W.1) writes: In the answer to "Any Questions?" of February 13, regarding the place hypotensive drugs have in the treatment of hypertension in pregnancy, you touch on the merits of (1) hexamethonium and tetraethylammonium compounds and on (2) hydrazinophthalazine, thiophanium, and veratrone. In connexion with the neurogenic factor in hypertension Mendlowitz has classified the site of therapeutic action of hypotensive drugs at four levels.[1] (*a*) The cortical, where barbiturates and rauwolfia serpentina act; (*b*) the hypothalamic, affected by protoveratrine and 1-hydrazinophthalazine corresponding to group (2) above; (*c*) the ganglionic level which reacts to the hexamethonium compounds, equivalent to the classification (1) above; and finally (*d*) the sympathetic nerve endings themselves. Rothlin[2] has shown that some portion of the pharmacological activity of the ergot derivatives is directed to the peripheral blocking of sympathico-adrenergic vasoconstrictor stimuli and that they have proved most useful for this purpose. The value of hypotensive drugs essentially needs to be considered along with the electrolyte NaCl, whose depletion appears to affect the non-neurogenic or intrinsic factor in hypertension, helping to reduce the blood pressure. The therapeutic agents in group (*b*) and (*d*) have a noticeable effect on the kidney. According to Moyer *et al.*,[3] 1-hydrazinophthalazine increases the renal blood flow in anaesthetized dogs. Simultaneous exhibition of adrenaline or *nor*adrenaline showed that this was a preferential decrease in peripheral resistance in the kidney to that in the extremities, in which there was no change in blood flow; while Willson and Smith[4] found that intravenous veratrone in the vagotomized animal heightened the perfusion rate of the isolated kidney. It is not improbable that the effectiveness of these therapeutic agents in toxaemia lies in the relief of an underlying renal ischaemia. Work on the ergot derivatives supports this view, as I mentioned recently in a letter in the *Lancet*.[5] I therefore feel that the barbiturates and the ergot derivatives should find inclusion in the reply and that the corollary of salt restriction needs emphasis.

REFERENCES

[1] Mendlowitz, M. (1953). *Ann. Intern. Med.*, **39**, 999.
[2] Rothlin, E. (1944). *Helv. physiol. acta*, **2**, C48.
[3] Moyer, J. H., Handley, C. A., and Huggins, R. A. (1951). *J. Pharmacol.*, **103**, No. 4, 368.
[4] Willson, J. R., and Smith, R. G. (1943). Ibid., **79**, 208.
[5] Sophian, J. (1954). *Lancet*, **1**, 107.

Correction.—In the obituary notice of Major-General W. H. S. Nickerson, V.C. (April 24, p. 989), we stated that he left Portsmouth Grammar School to become a medical student. This was a mistake, for it was from the Manchester Grammar School that he went on to Owens College.

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